Department of Plastic Surgery
Helsinki University Hospital
University of Helsinki
Finland

ONCOLOGICAL RESECTIONS AND RECONSTRUCTIONS OF THE CHEST WALL

JUHO SALO

ACADEMIC DISSERTATION

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Supervised by

Erkki Tukiainen, Professor of Plastic Surgery
Helsinki University Hospital
University of Helsinki
Finland

Reviewed by

Salvatore Giordano, Professor of Surgery
Turku University Hospital
University of Turku
Finland

Eero Sihvo, Docent
Jyväskylä Central Hospital
University of Helsinki
Finland

Opponent

Ilkka Koskivuo, Docent
Turku University Hospital
University of Turku
Finland

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ABSTRACT

Chest wall resection and reconstruction pose unique surgical challenges given the complex anatomy and important functional role of the chest wall and its protective function for vitally important organs. Yet, a paucity of literature has reported large patient series, likely attributable to the rarity of cases and the challenges posed by this complex surgical procedure. This thesis summarises a retrospective analysis of chest wall resections and reconstructions resulting from malignant disease. Here, the focus lies on the surgical outcomes, survival and quality of life amongst patients.

Study I consists of a retrospective review of patients who underwent oncological chest wall resection and reconstruction from 1997 through 2015 in the Department of Plastic Surgery at Töölö Hospital (Helsinki, Finland). The primary indications for resections were breast cancer, soft-tissue sarcoma and bone or chondrosarcoma. Amongst these resections, 53% were full- and 47% were partial-thickness resections, primarily located anterolaterally. Clear histological margins were reached in 82% of the resections. Reconstruction of the chest wall was warranted in 87% of cases and with 48% of cases involving stabilisation with a concurrent soft-tissue flap. The remaining patients underwent either chest wall stabilisation or soft-tissue flap coverage. This coverage most commonly consisted of pedicled or local flaps. Free flaps were necessary in 21% of cases, and no flaps were lost. Amongst 135 patients, 29 (21%) experienced complications. The most common complications included pneumonia and partial flap loss. We observed a 0% mortality rate. With a 4-year median follow-up, the 5-year overall survival rate reached 70%.

Study II describes our surgical technique for diaphragm and thoracoabdominal wall reconstruction following oncological resection, focusing here on surgical outcomes. The most common indication for surgery was sarcoma. A thoracoabdominal wall reconstruction was performed using mesh in 14 cases and 7 cases relied on mesh and a flap. A diaphragm reconstruction with a second mesh was warranted in 6 cases. In 15 cases, the diaphragm was reattached using an acceptable tension. Our method of thoracoabdominal wall and diaphragm reconstruction proved safe without abdominal wall hernias or paradoxical chest wall movement.

Study III evaluated the surgical outcomes, survival and tumour recurrence following chest wall resection amongst 49 soft-tissue sarcoma patients. Amongst these, 63% were high-grade and 37% were low-grade tumours. Surgery required 19 full- and 30 partial-thickness chest wall resections. The resection margins were wide or marginal in 86% of cases. The chest wall was stabilised and covered with soft tissue in 13 patients, reconstructed with a flap in 11, stabilised in 13 and closed primarily in 12. In total, 11 patients experienced complications. During follow-up, local recurrence developed in 8 patients and 9 patients developed metastasis. The 1-, 5- and 10-year survival rates were 93.8%, 76.0% and 71.6%, respectively. Recurrence-free rates were 84.4%, 70.7% and 70.7%, respectively. Positive prognostic factors consisted of being under 50 years old ($p = 0.01$), a wide margin ($p = 0.02$) and radical treatment ($p = 0.04$) consisting of either resection with a wide margin or a marginal resection combined with adjuvant radiotherapy. Patients undergoing nonradical treatment experienced a 3.1-fold reduction in survival compared to patients who underwent radical treatment (95% confidence interval [CI] 0.96–10.12; $p = 0.06$).

Cross-sectional study IV aimed to assess the long-term health-related quality of life (HRQoL) following chest wall reconstruction after oncological resection. In total, 78 patients who underwent surgery between 1997 and 2015 were invited to complete the 15D and Core Quality of Life for Cancer questionnaire (QLQ-C30) HRQoL instruments. Altogether, 55 patients (71%) completed the questionnaires, a median 66 ([IQR] 38–141) months after surgery. Indications for surgery included soft-tissue sarcoma (n = 16), advanced breast cancer (n = 15), bone or chondrosarcoma (n =14) or other tumour (n = 10). Following chest wall resection and reconstruction, the mean 15D score (0.878, standard deviation [SD] ±0.111) was comparable to that amongst the age- and gender-standardised general population (0.891, SD ±0.041). Patients were statistically significantly worse off on the dimensions of 'breathing' and 'usual activities'. The QLQ-C30 cancer-specific HRQoL was 72 (maximum 100) and scores for the QLQ-C30 functional scales ranged from 78 (physical) to 91 (social). Within specific reconstruction subgroups, no statistically significant differences in HRQoL were detected after analyses were adjusted.

In conclusion, chest wall resection and reconstruction represents a safe therapeutic modality when accompanied by careful patient selection, appropriate perioperative and postoperative care and selection of the proper surgical technique both in sarcoma and advanced breast cancer patients. Resection with wide margins remains the primary aim for treatment of chest wall soft-tissue sarcoma patients. If wide margins are not achieved, treatment should be combined with adjuvant radiotherapy. In locally advanced breast cancer, surgical chest wall resection and reconstruction have a certain role in the treatment of these patients. Following chest wall reconstruction after tumour resection, patients' HRQoL is comparable to that amongst the age- and gender-standardised general population.

Keywords: chest wall, resection, reconstruction, diaphragm, soft-tissue sarcoma, breast cancer, bone sarcoma, chondrosarcoma, health-related quality of life, 15D, QLQ-C30

TIIVISTELMÄ

Syöpäkasvaimen takia tehty rintakehän seinämän poisto- ja korjausleikkaus on haastava kirurginen toimenpide, koska seinämän anatomia on monimutkainen ja sillä on tärkeä toiminnallinen tehtävä hengityksessä ja elinten suojaamisessa. Aiheesta on aiemmin tehty vain muutamia laajoja potilasmääriä sisältäviä tutkimuksia, koska tapaukset ovat harvinaisia ja seinämän poisto kirurgisena toimenpiteenä on erittäin haastava. Tämän väitöskirjan tavoitteena oli arvioida pahanlaatuisten kasvaimien vuoksi tehtyjen rintakehän seinämän poisto- ja korjausleikkauksien kirurgisia menetelmiä ja niiden tuloksia sekä potilaiden selviytymistä ja elämänlaatua.

I osatyö oli takautuva tutkimus, joka koostui 135 potilaasta, joille tehtiin kasvaimen takia rintakehän seinämän poisto- ja korjausleikkaus Töölön sairaalan plastiikkakirurgian klinikalla vuosina 1997–2015. Pääsyyt leikkauksille olivat rintasyöpä, pehmytkudos- ja luusarkooma. Poistoleikkauksista 53% oli rintakehän seinämän kaikki kerrokset käsittäviä leikkauksia ja 47% vain osan kerroksista käsittäviä. Poistoleikkauksen yleisin anatominen sijainti oli rintakehän etusivuosa, ja 82%:ssa tapauksista poistoleikkauksen leikkausmarginaali oli kasvaimen suhteen puhdas. Rintakehän seinämän korjaaminen vaadittiin 118 tapauksessa, joista 48%:ssa tarvittiin luisen rakenteen vahvistaminen ja pehmytkudospuutoksen korjaus kielekkeellä. Osalle potilaista korjaukseksi riitti rintakehän vahvistaminen tai pehmytkudospuutoksen korjaus kielekkeellä. Kielekekorjauksista suurin osa oli paikallisia tai varrellisia kielekkeitä, mutta 21%:ssa tarvittiin mikrovaskulaarikieleke. Leikkaukseen liittyvää kuolleisuutta ei ilmentynyt eikä kielekkeen menetyksiä tapahtunut. 29 potilaalle tuli leikkauskomplikaatioita, joista yleisimmät olivat keuhkokuume ja kielekkeen kärkiosan menetys. Potilaiden leikkauksen jälkeinen mediaaniseuranta-aika oli yli 4 vuotta, ja 70% potilaista oli elossa 5 vuoden kuluttua leikkauksesta.

II osatyössä kuvattiin yhdistetyn rintakehän, vatsaontelon seinämän ja pallean korjausleikkauksen leikkaustekniikka syöpäkasvaimen poistoleikkauksen jälkeen ja arvioitiin niiden kirurgiset tulokset. Potilaita tutkimuksessa oli 21 ja yleisin syy leikkauksille oli sarkooma. 14 potilaalla rintakehän ja vatsaontelon seinämä pystyttiin korjaamaan verkolla ja seitsemällä potilaalla korjaus tehtiin verkolla ja kielekkeellä. Kuudelle potilaalle pallean korjaus tehtiin samassa yhteydessä toisella verkolla ja 15 potilaalla pallea oli mahdollista ommella uudelleen alkuperäiseen paikkaan hyväksyttävällä lihaskireydellä. Toimenpide todettiin tutkimuksessa turvalliseksi eikä sen jälkeen esiintynyt vatsan alueen tyriä tai rintakehän poikkeavaa liikettä.

III osatyössä tutkittiin 49 rintakehän seinämän sarkoomapotilaan leikkaustuloksia, taudin uusiutumista ja potilaiden selviytymistä. 63%:lla potilaista oli korkean ja 37%:lla matalan pahanlaatuisuuden asteen sarkooma. Rintakehän seinämän sarkooman poistoleikkaus käsitti 19 potilaalla kaikki rintakehän seinämän kerrokset ja 30 potilaalla osapaksuuden. 86%:lla potilaista poistoleikkauksen leikkausmarginaali oli laaja tai marginaalinen. Kasvaimen poiston jälkeisissä korjausleikkauksissa 13 potilaalle tehtiin rintakehän seinämän vahvistaminen ja kielekekorjaus, 11:lle kielekekorjaus, 13:lle rintakehän seinämän vahvistaminen ja 12 potilaalla leikkausalue pystyttiin sulkemaan suoraan. Komplikaatioita kehittyi 11 potilaalle. Seurannassa kahdeksalla potilaalla sarkooma uusiutui paikallisesti ja yhdeksällä potilaalla todettiin taudin etäpesäke. 1 vuoden kuluttua potilaista oli elossa 93.8%, 5 vuoden kuluttua 76.0% ja 10 vuoden kuluttua 71.6%. Tautivapaana potilaista oli 1 vuoden jälkeen oli 84.4%, 5 vuoden jälkeen 70.7% ja 10 vuoden jälkeen 70.7%. Potilaiden ennusteen kannalta suotuisia tekijöitä olivat alle 50 vuoden ikä ($p=0.01$), laaja leikkausmarginaali ($p=0.02$) ja radikaalihoito ($p=0.04$), joka tarkoittaa kasvaimen poistoleikkausta laajoilla leikkausmarginaaleilla tai marginaalisilla leikkausmarginaaleilla yhdistettynä liitännäissädehoitoon. Jos hoito ei ollut radikaali, potilaan ennuste oli 3.1 kertaa huonompi kuin radikaalihoidon saaneilla (95%CI 0.96-10.12; $p=0.06$).

IV osatyössä tutkittiin potilaiden elämänlaatua. 78 potilasta, joille oli tehty kasvaimen vuoksi rintakehän seinämän poisto- ja korjausleikkaus vuosien 1997–2015 aikana, pyydettiin täyttämään terveyttä ja elämänlaatua arvioivat 15D- ja QLQ-C30-kyselylomakkeet. 55 potilasta (vastausprosentti 71%) vastasi kysymyslomakkeisiin. Heistä 16 oli leikattu pehmytkudossarkooman, 15 paikallisesti edenneen rintasyövän tai rintasyövän uusiutuman/etäpesäkkeen, 14 rusto/luusarkooman ja 10 muiden kasvaimien vuoksi. Mediaani vastausaika leikkaustoimenpiteestä oli 66 ([IQR] 38–141) kuukautta. Kasvaimen vuoksi tehdyn rintakehän seinämän poisto- ja korjausleikkauspotilaiden 15D elämänlaatuinstrumentin pisteiden keskiarvo (0.878, SD 0.111) oli vertailukelpoinen ikä- ja sukupuolivakioituun väestöön (0.891 SD 0.041) verrattuna. 15D-elämänlaatukysymyksissä potilaat saivat huonommat pisteet “hengitys”- ja ”tavalliset aktiviteetit” -osa-alueista. QLQ-Q30-mittarilla syöpäspesifiset elämänlaatupisteet olivat 72 (maksimi 100) ja toiminnallisessa asteikossa ne vaihtelivat 78:sta (fyysinen) 91:een (sosiaalinen). Korjausleikkausmenetelmällä ei ollut tilastollisesti merkitsevää vaikutusta potilaan elämänlaatuun kummallakaan elämänlaatumittarilla mitattuna.

Yhteenvetona todetaan, että huolellisella potilasvalinnalla, hyvällä suunnittelulla, virheettömällä leikkaustekniikalla ja täsmällisellä leikkauksen aikaisella ja jälkeisellä hoidolla laajakin rintakehän seinämän leikkaustoimenpide on turvallinen. Rintakehän seinämän sarkooman hoidossa tavoitteena on kasvaimen poisto laajallakin marginaalilla, ja jos tätä ei saavuteta, tulisi hoitoa täydentää sädehoidolla. Myös paikallisesti levinneen rintasyövän hoidossa tällä leikkausmenetel-

mällä on paikkansa. Rintakehän seinämän kasvaimen poisto- ja korjausleikkausten jälkeen potilaiden elämänlaatu on vastaava kuin ikävakioidun vertailuväestön.

Avainsanat: rintakehän seinämä, resektio, rekonstruktio, pallea, pehmytkudossarkooma, rintasyöpä, kondrosarkooma, luusarkooma, elämänlaatu, 15D, QLQ-C30

CONTENTS

LIST OF ORGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals.

I Salo JTK, Tukiainen EJ. Oncologic Resection and Reconstruction of the Chest Wall: A 19-Year Experience in a Single Center. *Plast Reconstr Surg.* 2018 Aug;142(2):536–547.

II Kuwahara H, Salo J, Tukiainen E. Diaphragm reconstruction combined with thoraco-abdominal wall reconstruction after tumor resection. *J Plast Surg Hand Surg.* 2018 June;52(3):172–177.

III Kuwahara H, Salo J, Nevala R, Tukiainen E. Single-Institution, Multidisciplinary Experience of Soft Tissue Sarcomas in the Chest Wall. *Ann Plast Surg.* 2019 July;83(1):82–88.

IV Salo JTK, Repo JP, Roine RP, Sintonen H, Tukiainen EJ. Health-related quality of life after oncological resection and reconstruction of the chest wall. *J Plast Reconstr Aesthet Surg.* 2019 Nov;72(11):1776–1784.

ABBREVIATIONS

ADM	Acellular dermal matrix
ALT	Anterolateral thigh flap
A-V	Aterio-venous
BMI	Body mass index
CCI	Charlson comorbidity index
CD	Clavien–Dindo classification
CTA	Cephalic vein–thoracoacromial artery
DFS	Disease-free survival
DFSR	Disease-free survival rate
DIEP	Deep inferior epigastric artery perforator
EORTC	The European Organisation for Research and Treatment of Cancer
EUROCARE	European Cancer Registry–based study
FEV	Forced expiratory volume
FEV1	Forced expiratory volume in 1 second
FEV%	Ratio of FEV1 to forced vital capacity
FNCLCC	French Federation Cancer Centre
FVC	Forced vitality capacity
G-CSF	Granulocyte stimulating factor
HRQoL	Health-related quality of life
ICAP	Intercostal artery perforator
ICU	Intensive care unit
IQR	Interquartile range
LRFS	Local recurrence-free survival
MDT	Multidisciplinary team
MMA	Methylmethacrylate
MMS	Methylmethacrylate ‘sandwich’ technique
OS	Overall survival
PEEK	Polyetheretherketone
PMMA	Polymethylmethacrylate
PP	Polypropylene
PTFE	Polytetrafluoroethylene
QLQ-C30	Core Quality of Life questionnaire C30
QOL-CS	Quality of Life for Cancer Survivors
RAS	Robot-assisted surgery
RT	Radiation therapy
SD	Standard deviation
SEAP	Superior epigastric artery perforator

SF-36	Short-Form 36
TDAP	Thoracodorsal artery perforator flap
TFL	Tensor fascia lata muscle flap
TRAM	Transversal rectus abdominis muscle flap
UICC	Union for International Cancer Control
UPS	Undifferentiated pleomorphic sarcoma
VRAM	Vertical rectus abdominis muscle

1 INTRODUCTION

Chest wall reconstruction is indicated for the correction of defects caused by tumour resection, radiation necrosis, infection, trauma or congenital deformities (Arnold, Pairolero 1996, Tukiainen 2013). Oncologic resection may be attributed to a primary, locally invading or metastatic tumour. The most common primary malignancies consist of bone and chondrosarcomas and soft-tissue sarcomas, whilst advanced breast and lung cancer can both invade the chest wall. In addition, cancer metastases could develop in the chest wall (Losken, Thourani et al. 2004, Mansour, Thourani et al. 2002).

The primary aim of curative treatment is complete tumour resection. Oncological resection should not be compromised based on a fear of a chest wall or diaphragm defect following resection. An isolated diaphragm resection is quite rare, given the rarity of primary or secondary tumours of the diaphragm (Baldes, Schirren 2016). Typically, diaphragm resection and reconstruction are combined with thoracoabdominal wall tumour resection and reconstruction, lung cancer or mesothelioma surgery (Mansour, Thourani et al. 2002).

Chest wall defects can be either full- or partial-thickness. Reconstruction features two aspects: stabilisation and soft-tissue reconstruction or coverage. Synthetic meshes have remained the primary means of stabilisation for many years (Arnold, Pairolero 1996). The aims of chest wall reconstruction consist of achieving an airtight closure, maintaining adequate respiratory function, avoiding lung herniation, protecting vital intrathoracic organs and creating a stable platform for the shoulders and upper extremities (Tukiainen 2013, Mahabir, Butler 2011, Althubaiti, Butler 2014, Thomas, Brouchet 2010). Reconstruction should also achieve sufficient stability allowing physiological movements and obliterating the dead space in the chest wall cavity (Bakri, Mardini et al. 2011, Netscher, Baumholtz 2009, Harati, Kolbenschlag et al. 2015).

With the available flap coverage techniques, wider surgical resection margins and, thus, better local tumour control can be achieved (Althubaiti, Butler 2014, Arnold, Losken, Thourani et al. 2004). The size and location of the chest wall defect, the availability of local and pedicled flaps, previous operations or radiotherapy and the general condition and prognosis of the patient impact the choice of soft-tissue flap reconstruction. The first choice is a pedicled myocutaneus flap. The second choice, if pedicled flaps are inadequate in terms of dimensions or unavailable, is a microvascular free flap (Arnold, Pairolero 1996, Tukiainen 2013).

The diaphragm separates the thoracic and abdominal cavity. Reconstruction must maintain the volume of the chest wall cavity, restore proper respiratory functioning and prevent herniation (Gaissert, Wilcox 2016). In small defects, primary closure is possible. However, a too-tight primary closure results in a flat drum-head diaphragm with incomplete functioning (Bax, Collins 1984). In large or complete resections of the diaphragm, reconstruction with synthetic material or autologous tissue represents the optimal choice (Finley, Abu-Rustum et al. 2009).

In recent decades, cancer studies have included health-related quality-of-life (HRQoL) measurements as an endpoint (Bottomley, Aaronson et al. 2007). As a patient-reported outcome, HRQoL provided by a patient can be used to understand a patient's opinion concerning their mental, emotional, physical and social well-being. Until recently, information on long-term HRQoL following oncological chest wall resection and reconstruction has remained limited (Wakeam, Acuna et al. 2017).

Extensive chest wall resection and reconstruction are surgically challenging procedures, which may also be life-threatening to the patient. For this reason, a careful multidisciplinary approach in patient selection and treatment is crucial. In addition, careful perioperative and postoperative therapy is essential to achieving the optimal and earliest possible recovery (Tukiainen 2013).

This doctoral thesis was initiated to investigate the surgical outcomes, survival and HRQoL following chest wall reconstruction after oncological resection. In the first study, we focused on survival and surgical outcomes following chest wall resection and reconstruction. The second study focused on the surgical method in chest wall reconstruction combined with diaphragm reconstruction. The third study evaluated survival, disease-free survival, surgical outcomes and prognostic factors amongst soft-tissue sarcoma patients following chest wall resection and reconstruction. Finally, the fourth study assessed the long-term HRQoL amongst patients following chest wall reconstruction after oncological resection.

2 REVIEW OF THE LITERATURE

2.1 A history of chest wall resections and reconstructions

Chest wall resections have long traditions, procedures which posed a challenge surgeons approached apprehensively for over 200 years. The first known chest wall resection for a tumour was reported in 1778 by Osias Aimar, who resected an osteosarcoma of the ribs. In 1881, von Speicher in a literature review summarised 28 cases, only a few of which were treated surgically (Hedblom 1921).

In the late 1800s, Fell and O'Dwyer described intubation techniques and positive-pressure ventilation (O'Dwyer 1887, Fell 1891). Subsequently, in 1898, Parham reported two successful chest wall resections, during the second of which he used an endotracheal tube to stabilise ventilation (Parham, 1899). A very high incidence of complications and a 20% to 30% mortality rate were reported at the beginning of the twentieth century in chest wall resections. Despite these grim figures, in the 1910s and 1920s, reports of chest wall resections increased (Hedblom 1933).

In 1906, Tansini described for the first time the use of a muscle flap. He covered an anterior chest wall defect after radical mastectomy using a latissimus dorsi muscle flap (Tansini 1906).

The modern era of chest wall resection really began in the late 1940s, thanks to improvements in surgical techniques and anaesthesia, antibiotics, critical care and the development of new reconstruction techniques (Meyerson Shari, Harpole Jr David 2009, Book of General thoracic Surgery).

In the 1940s, Watson and James introduced the use of avascular fascia lata grafts in chest wall reconstructions (Watson, James 1947). Maier treated large anterior defects with local cutaneous flaps including the mobilisation of the remaining breast as coverage (Maier 1947). Bisgard and Swenson described the first use of rib grafts for chest wall reconstruction following sternal resection (Bisgard, Swenson 1948). The late 1950s witnessed the development of appropriate alloplastics, and Usher et al. introduced the Marlex mesh (Usher 1959).

Tansini was the first to use the latissimus dorsi muscle flap for a partial-thickness defect. But, in the 1950s, Campbell introduced the reconstruction of anterior full-thickness chest wall defects using a latissimus dorsi muscle flap and a split-thickness skin graft (Campbell 1950). In addition, Kiricuta first described the use of an omentum flap for the reconstruction of the chest wall (Kiricuta 1963).

Methods for soft-tissue reconstruction then went unnoticed for nearly 20 years until interest in muscle flaps was revived by McCormack et al. (McCormack, Bains et al. 1981), Larson et al. (Larson, McMurtrey et al. 1982) and Arnold and Pairolero (Pairolero, Arnold 1985), who all published large patient series.

2.2 Anatomy of the thorax and chest wall

The thorax is the cavity of the body surrounded by the chest wall, containing the heart, lungs, esophagus, trachea, thoracic duct, thymus and great vessels. Caudally, the diaphragm separates the thoracic and abdominal cavities. Cranially, the thorax communicates with the neck and upper extremities. The chest wall protects vital organs in the thoracic cavity, enabling the generation of negative pressure required for respiration (Roberts Kenneth, Weinhaus 2015)(Handbook of Cardiac Anatomy, Physiology and Devices).

2.2.1 Thoracic skeleton

The thoracic skeleton of the thoracic cage consists of 12 ribs and the costal cartilage, the thoracic vertebrae and the sternum **(Figure 1)**. The sternum consists of three parts: the manubrium, body and xiphoid process. In the anterior part of the chest wall, the first seven rib pairs are attached to the sternum. The next three are attached to each other by the costal cartilage and to the seventh rib. The eleventh and twelfth ribs 'float', remaing unconnected to the sternum (Clemens, Evans et al. 2011). The bones of the pectoral girdle, scapula and clavicle are attached to the thorax. The thoracic outlet to the upper arm is formed by the clavicle and the first rib (Roberts Kenneth, Weinhaus 2015)(Handbook of Cardiac Anatomy, Physiology and Devices). Major structures pass to the head and upper extremity through the thoracic inlet surrounded by the manubrium, the first thoracic vertebrae and the first ribs (Meyerson Shari, Harpole Jr David 2009)(Book General thoracic Surgery).

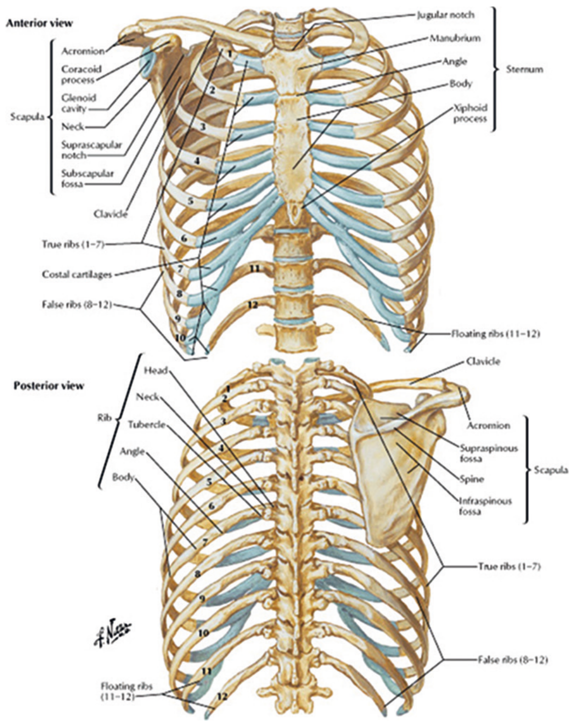

Figure 1. Anatomy of the thoracic skeleton. *Netter illustration used with permission of Elsevier, Inc. All rights reserved.*

2.2.2 Muscles of the thoracic wall

Several superficial muscles of chest wall create part of the thorax contour and accomplish shoulder movements **(Figure 2)**. These muscles, including the pectoralis major, pectoralis minor, anterior part of the deltoid, latissimus dorsi, subclavius and serratus anterior, are attached to the clavicle, shoulder girdle and humerus. Some of these muscles also play a role in respiratory movements (Roberts Kenneth, Weinhaus 2015)(Handbook of Cardiac Anatomy, Physiology and Devices). In addition, other muscles are attached to the chest wall including the abdominal muscles, and some neck and back muscles.

The diaphragm is the most important muscle for respiration, referred to as the primary muscle of inspiration, innervated by the phrenic nerves (Meyerson Shari, Harpole Jr David 2009)(Book General thoracic Surgery).

The intercostal space consists of three muscle layers: the external intercostal muscle, the internal intercostal muscle and the innermost intercostal muscle. The deepest muscle layer comprises the the innermost intercostal muscle, the subcostal muscles and the transverse thoracic muscles (Meyerson Shari, Harpole Jr David 2009)(Book General thoracic Surgery).

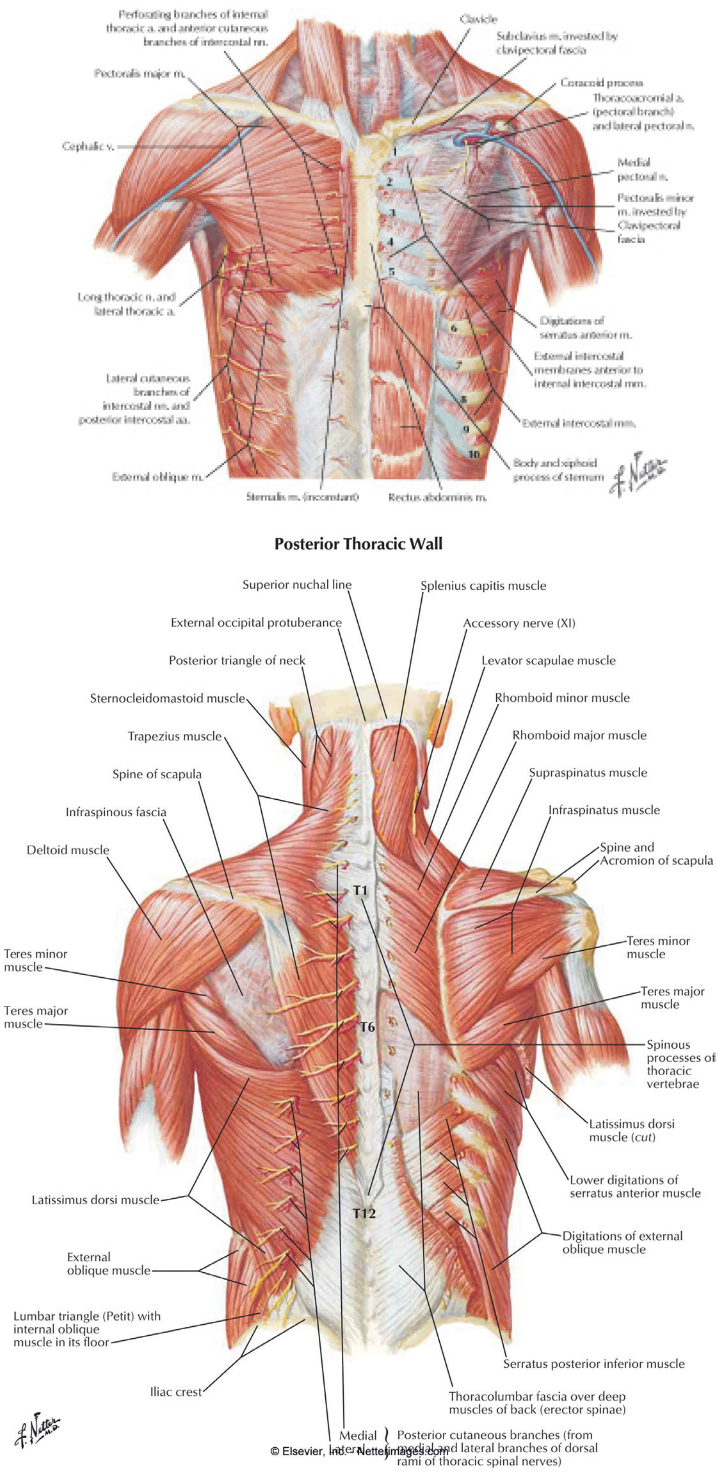

Figure 2. Anterior and posterior anatomy of the thorax wall. *Netter illustration used with permission of Elsevier, Inc. All rights reserved.*

2.2.3 Vascular supply of the chest wall

The chest wall arterial supply is received from both subclavian arteries and the thoracic aorta **(Figures 3 and 4)**. The internal thoracic arteries run along both sides, lateral to the sternum and posterior to the costal cartilages, giving rise to the anterior intercostal arteries before diverging to the superior epigastric and the musculophrenic arteries. The superior epigastric artery anastomoses with the inferior epigastric artery in the abdominal wall (Saxena, Alalayet 2017)(Book, Chest wall deformities). The first two intercostal arteries are branches of the superior intercostal arteries, supplied by the axillary artery. The posterior side of the thoracic aorta supplies the posterior intercostal arteries and the subcostal arteries. The posterior intercostal arteries anastomose with the anterior intercostal arteries, creating an anastomotic network of the thoracic wall (Roberts Kenneth, Weinhaus 2015)(Handbook of Cardiac Anatomy, Physiology and Devices).

The axillary artery gives rise to the superior thoracic artery, the thoracoacromial artery and the lateral thoracic artery. In addition to the first and second intercostal space, the superior thoracic artery supplies the superior part of the anterior serratus (Saxena, Alalayet 2017)(Book, Chest wall deformities). The lateral thoracic artery supplies the rest of the serratus anterior muscle. The thoracoacromial artery gives rise to the pectoral, deltoid, clavicular and acromial branches, which supply the pectoral muscles, the deltoid muscle, the clavicle and the subclavius muscle. The diaphragm is supplied by the musculophrenic artery, the distal part of the internal thoracic artery and blood supply from the inferior side, specifically from the inferior phrenic artery and the superior branches of abdominal aorta (Roberts Kenneth, Weinhaus 2015)(Handbook of Cardiac Anatomy, Physiology and Devices).

The chest wall is drained by the anterior and posterior intercostal veins accompanied by the intercostal arteries. The first six anterior intercostal veins are drained into the internal thoracic vein, which drains into the subclavian vein. The distal intercostal veins are drained into the musculophrenic veins. The posterior intercostal veins drain into the azycos venous system and further into the superior vena cava (Saxena, Alalayet 2017)(Book, Chest wall deformities).

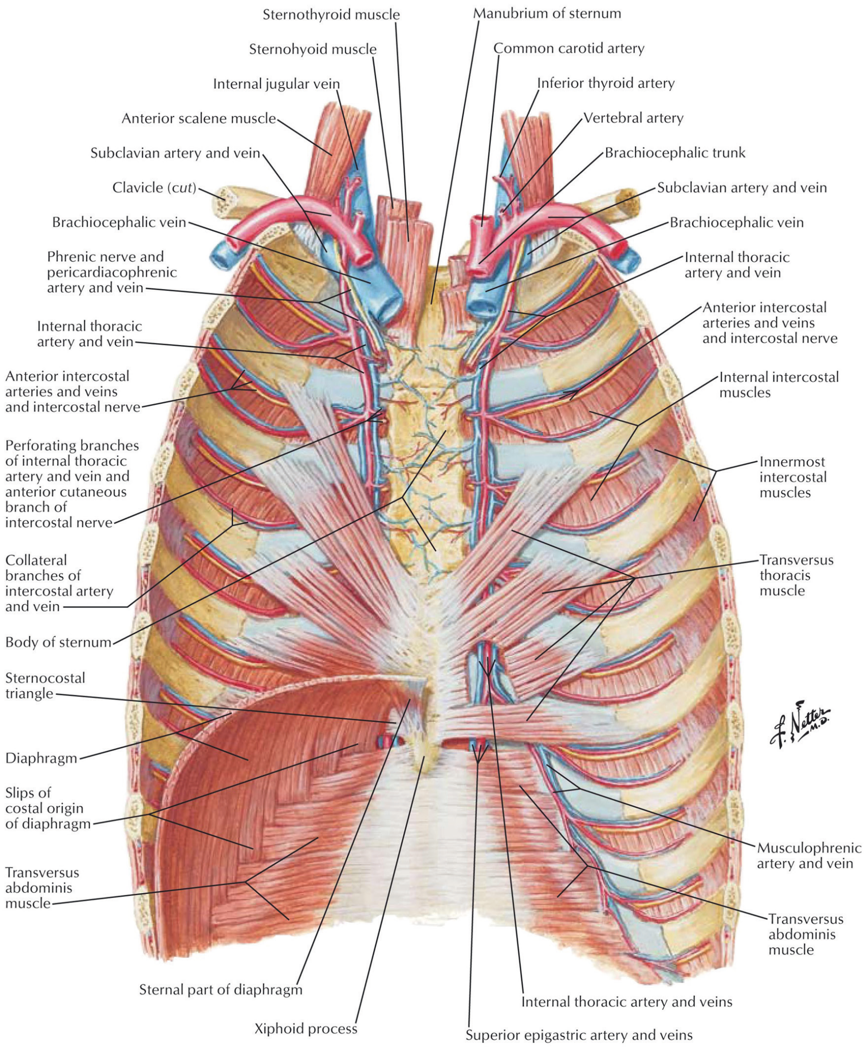

Figure 3. Internal view of the chest wall anatomy. *Netter illustration used with permission of Elsevier, Inc. All rights reserved.*

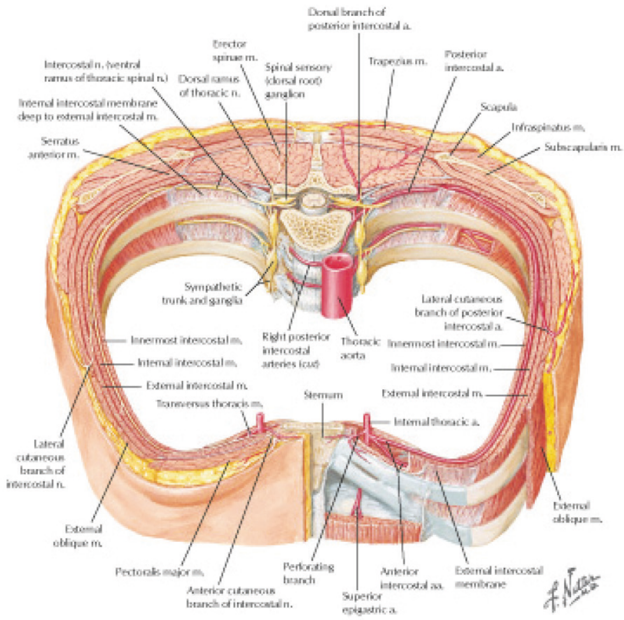

Figure 4. Plane anatomy of the chest wall. Netter illustration used with permission of Elsevier, Inc. All rights reserved.

2.2.4 Nerves of the thoracic wall

The chest wall is innervated by 12 pairs of thoracic spinal nerves formed from the dorsal (sensory neurons) and ventral (somatic motor neurons) roots. These roots form the mixed spinal nerve. After the intervertebral foramen, the spinal nerve is further divided into the anterior (ventral) and posterior (dorsal) ramus. The posterior ramus supplies the paravertebral back muscles and the skin of the dorsal area. After the intervertebral foramen, the anterior ramus establishes communication with the sympathetic nerves forming the intercostal nerve. The branch of the intercostal nerve leads to the collateral branch, the lateral cutaneus branch, the anterior cutaneus branch, the muscular branches, the communicating branches and the peritoneal sensory branches. These branches of intercostal nerves innervate muscles (intercostal, subcostal, serratus posterior and transverse thoracic muscles), segmental skin areas and the pleural and superior peritoneal membranes (Saxena, Alalayet 2017, Meyerson Shari, Harpole Jr David 2009) (Book, Chest wall deformities, Book General thoracic Surgery).

2.2.5 Lymphatic drainage of the thoracic wall

The lateral and posterolateral intercostal spaces are drained by lymphatics, which enter the lymph nodes near the vertebral ends of the intercostal space. The superior nodes drain into the thoracic duct and the inferior nodes drain into the cisterna styli. The anterior intercostal space drains into the parasternal internal nodes (Saxena, Alalayet 2017)(Book General thoracic Surgery). The thoracic duct is the main lymphatic duct of the body, 38- to 45-cm-long running between the aorta and the azygos vein from the cisterna chyli to the superior and emptying into the junction of the internal jugular veins and the left subclavian. The thoracic duct is responsible for the lymph drainage from the entire body, except for the right sides of the head, neck, thorax and the right upper extremity. An iIatrogenic surgical injury of the thoracic duct could result in a chylothorax (Ilahi, St Lucia et al. 2020).

2.2.6 Pleura

The pleural cavity is formed by the visceral and parietal pleurae of the lungs. Pleurae are serous membranes, forming a two-layer membranous structure. Normally, the thin space between the two pleural layers is called the pleural cavity, which contains a small amount of pleural fluid. The outer pleura (parietal pleura) is attached to the chest wall and the inner pleura (visceral pleura) covers the lungs and adjoining structures, via blood vessels, bronchi and nerves. The visceral pleura lacks sensory innervations, whilst the parietal pleurae are quite sensitive to pain (Charalampidis, Youroukou et al. 2015).

The pleural space plays an important role in respiratory function. Negative intrapleural pressure generated by the respiratory muscles expands the lungs, and physically a small amount of intrapleural fluid maintains the mechanical coupling between the pleural surfaces (Negrini, Moriondo 2013).

2.3 Respiratory function

2.3.1 Inspiration

Chest wall movement and respiration can be divided into active and passive events. Inspiration and the enlargement of the chest cavity represent active events caused by the contraction of the diaphragm, and the internal and external intercostal muscles (primary inspiratory muscles). During deeper inspiration, the scalene and sternocleidomastoid muscles act as secondary accessory muscles of inspiration (**Figure 5**). The enlarged thorax dimensions reduce intrathoracic, intrapleural and intrapulmonic pressure and, therefore, draw air into the lungs.

2.3.2 Expiration

Expiration is primarily a passive event, caused by the elastic recoil of the lungs and the chest wall. During active expiration, the lateral internal intercostal muscles and abdominal muscles are also used (**Figure 5**). During laboured breathing, other skeletal muscles can be applied (Meyerson Shari, Harpole Jr David 2009, Roberts Kenneth, Weinhaus 2015)(Book General thoracic Surgery, Handbook of Cardiac Anatomy, Physiology and Devices).

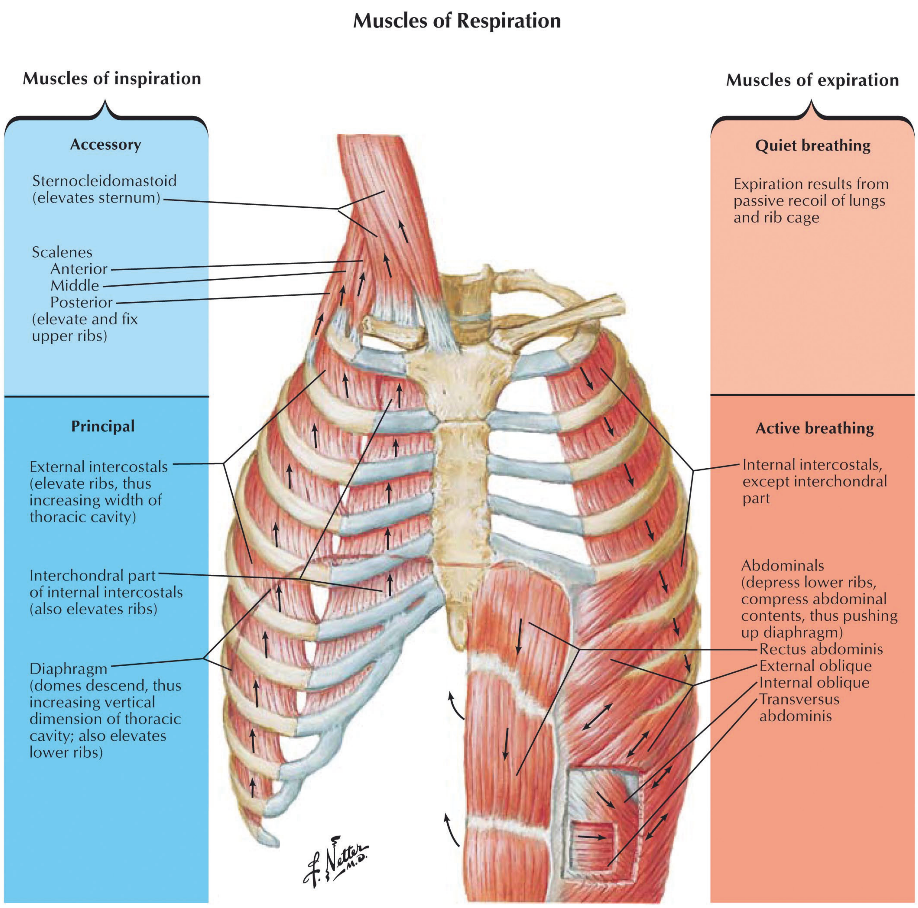

Figure 5. The muscles of respiration. *Netter illustration used with permission of Elsevier, Inc. All rights reserved.*

2.3.3 FEV1, FEV AND FEV%

Pulmonary functioning tests are used to study the suitability of a patient for surgery or the possible impact of an operation. FEV1 refers to the forced expiratory volume in 1 s. Forced vital capacity (FVC) refers to the maximum volume of air that can be expired. FEV% refers to the proportion of FVC expired in the first second (Clemens, Evans et al. 2011). FEV1 and FVC have been shown to decrease slightly following chest wall resection and reconstruction, averaging from 5.1% to 18.2% (Corkum, Garvey et al. 2020, Daigeler, Druecke et al. 2009).

2.4 Tumours requiring oncological chest wall resection and reconstruction

Chest wall reconstruction may be indicated for defects resulting from a tumour resection, radiation necrosis, infection, trauma or congenital deformities (Arnold, Pairolero 1996, Tukiainen 2013). The treatment strategy for traumatic defects and postoperative infections is different, typically handled separately in the literature (Althubaiti, Butler 2014), which lie beyond the scope of this dissertation.

Oncological chest wall tumour resection may be attributed to a primary, locally invading or metastatic tumour. The most common oncological indications for chest wall resection are bone and chondrosarcomas, soft-tissue sarcomas, advanced breast cancer and lung cancer as well as cancer metastases (Losken, Thourani et al. 2004, Mansour, Thourani et al. 2002).

2.4.1 Soft-tissue sarcoma

Sarcomas are rare malignant tumours originating from mesenchymal cells, consisting of a heterogenous group of tumours, including over 80 different histological subtypes (Fletcher, Bridge et al. 2013). The incidence of soft-tissue sarcoma in the European Cancer Registry–based study (EUROCARE) was 5.6/100 000 (Stiller, Trama et al. 2013).

The most common histological types include liposarcoma and leiomyosarcoma (Stiller, Trama et al 2013). The aetiology of these tumours remains generally unknown. In rare cases, ionising radiation has been shown to induce sarcomas. Secondary sarcomas in the chest wall in breast cancer patients are overrepresented due to radiation therapy. The incidence of radiation-associated angiosarcoma has increased following breast-conserving surgery (partial mastectomy following radiation therapy) (Salminen, Sampo et al. 2018). The definition of postradiation sarcoma is a history of radiation therapy (RT), a latency period of several years following RT, the occurrence of a sarcoma in an irradiated field and histology for a sarcoma distinct from the primary cancer (Cahan et al. 1948). The most common postradiation sarcomas consist of malignant fibrous histiocytoma (now known as undifferentiated pleomorphic sarcoma or UPS) and osteosarcoma (Wiklund et al. 1991). A heterogenous group of soft-tissue sarcomas comprise UPSes. In these tumours, no specific cell-line differentiation is observed (Fletcher, Bridge et. al. 2013). Two sarcoma grading systems are widely used: the French Federation of Cancer Centre's (FNCLCC) grading system, which consists of three grades (grade I low, grade II high and grade III high) (Guillou, Coindre et al. 1997, Trojani, Contesso et al. 1984) and a four-grade system used in Scandinavia (Markhede, Angervall et al. 1982, Meis-Kindblom, Bjerkehage et al. 1999), which we used in this thesis. In the Scandinavian four-grade system, I and II represent low-grade tumours, whilst III and IV are high-grade tumours.

Sarcomas emerge most often in the lower extremities. The trunk wall is the anatomical site of these tumours in less than 14% of cases, and only a portion of these occur in the chest **(Figure 6)** or the thoracoabdominal wall (Mastrangelo, Coindre et al. 2012).

Surgical treatment and local control of soft-tissue sarcomas are based on wide surgical margins. If wide margins are not achieved, radiotherapy is recommended (Sampo, Tarkkanen et al. 2008). Postoperative radiotherapy in a randomised trial by Yang et al. reduced the incidence of local recurrence in high-grade sarcomas, but did not improve survival (Yang, Chang et al. 1998). The role of adjuvant chemotherapy remains controversial, with protocols varying between sarcoma centres. In a recent meta-analysis, chemotherapy appeared to reduce the distant recurrence rate and improve survival (Pervaiz, Colterjohn et al. 2008). Currently, soft-tissue sarcoma patient 5-year relative survival rates stand at 60% (Stiller, Botta et al. 2018).

Figure 6. (Above, left) Chest wall soft-tissue sarcoma. (Above, middle) Lateral, full-thickness chest wall resection. (Above, right) Chest wall stabilisation using a sandwich technique (methylmethacrylate between two meshes). (Below, left) Soft-tissue reconstruction with a free anterolateral thigh (ALT) flap. (Below, right) One week postoperative.

2.4.2 Bone sarcoma

Primary malignant bone tumours (bone sarcomas) remain quite rare, and include osteosarcoma, chondrosarcoma, chordoma and Ewing sarcoma. The most common types consist of osteosarcoma and chondrosarcoma, both of which have an incidence of 0.2/100 000 in Europe (Stiller, Trama et al. 2013). Among chondrosarcomas and osteosarcomas, 13.6% and 3.2%, respectively, occur in the chest wall area (Damron, Ward et al. 2007). The treatment of osteosarcoma is neoadjuvant chemotherapy followed by surgical resection and adjuvant chemotherapy. Chondrosarcoma is curatively treated with en-bloc resection (Casali, Bielack et al. 2018).

2.4.3 Locally advanced breast cancer

In 2018, breast cancer was one of the most common malignancies in women, with 2.1 million new breast cancers diagnoses occurring in the world. In Europe, age-adjusted annual incidence of breast cancer reached 144.9/100 000 (Cardoso, Kyriakides et al. 2019). Overall survival is primarily influenced by the stage of disease. In the twenty-first century, relative 10-year survival of breast cancer reached 89% for local disease, 62% for regional disease and 10% for metastatic disease in Europe (Allemani, Minicozzi et al. 2013). Locally advanced breast cancer involving the chest wall may consist of primary, recurrent **(Figure 7)** or metastatic disease (Ahmad, Yang et al. 2015). Most often, chest wall–related breast cancer manifests in local recurrent with or without metastatic disease (D'Aiuto, Cicalese et al. 2010).

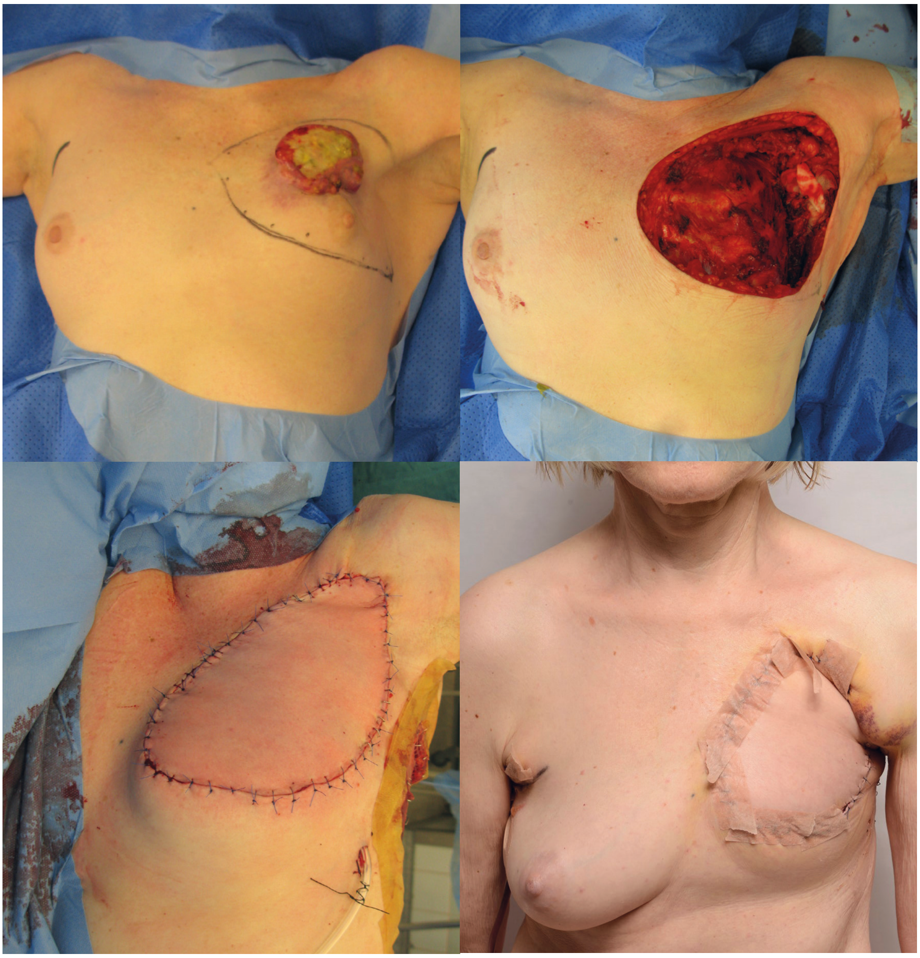

Figure 7. (Above, left) Chest wall recurrence of breast cancer. (Above, right) Anterolateral partial-thickness chest wall resection. (Below, left) Soft-tissue reconstruction with a pedicled musculocutaneus latissimus dorsi flap. (Below, right) One week postoperatively.

2.4.4 Lung cancer

Lung cancer is the leading cause of cancer death in the world, resulting in 1.4 million deaths in 2008 (Jemal, Bray et al. 2011). Tumour invasion to the chest wall is in about 5-8% of operatively treated lung cancer patients (Stoelben, Ludwig 2009, Voltolini, Rapicetta et al. 2006). In chest wall invasive lung cancer without distant metastasis, treatment invovles surgical lung and chest wall R0 resection (Riquet, Arame et al. 2010). Lung cancer that invades the parietal pleura or chest wall at the level of the second rib or above is referred to as a Pancoast tumour. Resection of these tumours poses challenges given infiltration of the tumour to the chest wall, as well as to the subclavian vessels and plexus. Treatment for a Pancoast tumour relies on neoadjuvant radiochemotherapy combined with surgical resection (Stoelben, Ludwig 2009). According to existing studies, a lung cancer patient with chest wall invasion treated with en-bloc lung and chest wall resection can expect 5-year overall survival rates varying from 18% to 61% (Lanuti 2017). In lymph node–negative chest wall–involved lung cancer, 5-year overall survival increases to 67% (Facciolo, Cardillo et al. 2001).

2.4.5 Others

2.4.5.1 Other primary tumours

Many other rare malignant and benign tumours are mentioned in the literature related to chest wall resection. For example, Chang et al. mentioned squamous cell carcinoma patients (Chang, Mehrara et al. 2004) and Daigler et al. (Daigeler, Druecke et al. 2009) included angiomyolipoma in their patient series.

2.4.5.2 Secondary malignant tumours (metastases)

Improvements to cancer treatment have increased survival in many types of cancer in recent years. Because even metastatic disease can be controlled through oncological treatment in some of these malignancies, surgical operation for solitary chest wall metastasis represent valid options (David, Marshall 2011). The most common surgically treated chest wall metastases derive from melanoma, colorectal carcinoma, renal cancer and cervical cancer (Daigeler, Druecke et al. 2009, Weyant, Bains et al. 2006, Dudek, Schreiner et al. 2018).

2.5 Classification of the anatomical location of chest wall resections

The anatomical classification of chest wall resections remains lacking. Our classification is described in **Figure 8** (Kuwahara, Salo et al. 2018). Some authors use the following classification: anterior, lateral, anterior lateral, posterior, posterior lateral and forequarter (Weyant, Bains et al. 2006).

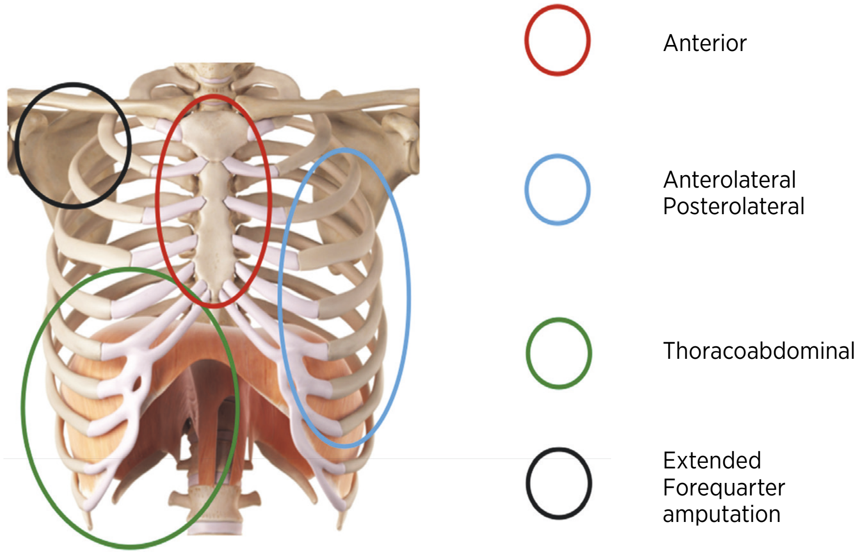

Figure 8. Classification of the anatomical location of chest wall resections (Kuwahara, Salo et al. 2018).

2.6 Oncological resection of the chest wall and diaphragm

2.6.1 Chest wall resection

The aim of tumour resection is the complete tumour resection, representing the most important prognostic factor in tumour surgery. The definition of a complete resection is not uniform in surgical oncology. The R classification represents one the most commonly used methods for reporting these surgical margins. The R classification denotes the presence of any residual tumour following surgery or treatment (see **Table 1**). This classification considers the residual tumour at the primary tumour site, in the logoregional lymph nodes and in distant metastases (Hermanek Paul, Sobin et al. 1987). Enneking's classification system is widely used to report the surgical margins of soft-tissue sarcoma (Enneking, Spanier et al. 1980), summarised in **Table 2.** In this thesis, in soft-tissue sarcoma surgery, Enneking´s classification system has been used to categorise the surgical margins.

Table 1. The R classification of surgical margins.

RX	The presence of residual tumour cannot be assessed
R0	No residual tumour
R1	Microscopic residual tumour
R2	Macroscopic residual tumour

Table 2. Enneking´s classification system of surgical margins.

Intralesional	Tumour present at the margin
Marginal	Pseudocapsule present at the margin
Wide	Histologically nonreactive normal tissue at the margin
Radical	All normal tissue of the involved anatomical compartment excised *en bloc*

The R0 resection (microscopically negative margins) represents the primary target of surgical treatment in a curative as well as in a palliative setting whenever possible. In some resections with a palliative intent, R1 and R2 resections may be mandatory and acceptable because of the clinical situation. Oncological resection should not be compromised due to a fear of chest wall defect following resection.

The histology of the tumour defines the resection margins (Harati, Kolbenschlag et al. 2015). However, different centres have adopted varying definitions of the surgical margins to guide their clinical practices. The resection in the chest wall can be partial thickness **(Figure 9 and 10)** or full thickness **(Figure 11)**. A full-thickness resection extends into all layers of the chest wall, whilst a partial-thickness resection includes either only soft-tissue resections or only skeletal bone resections (Tukiainen 2013). In some advanced cases, chest wall resection can be extended to include the lung, diaphragm, pericardium, clavicula or liver to achieve an R0 tumour removal (Arnold, Pairolero 1996).

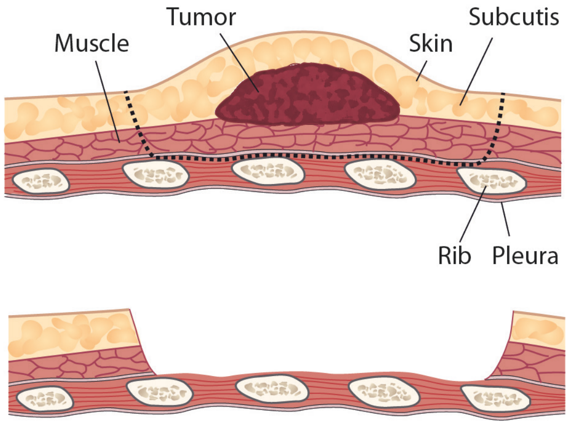

Figure 9. Partial-thickness chest wall resection (soft-tissue resection).

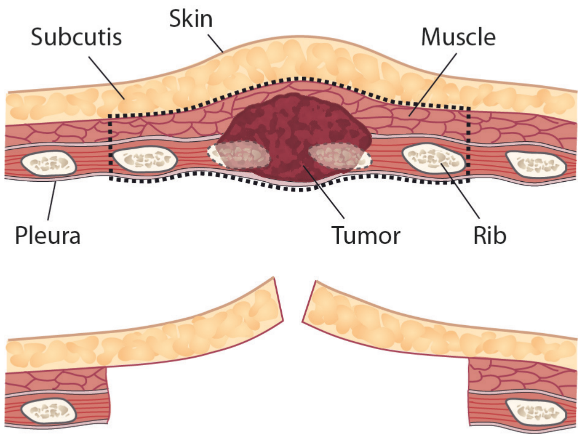

Figure 10. Partial-thickness chest wall resection (skeletal bone resection).

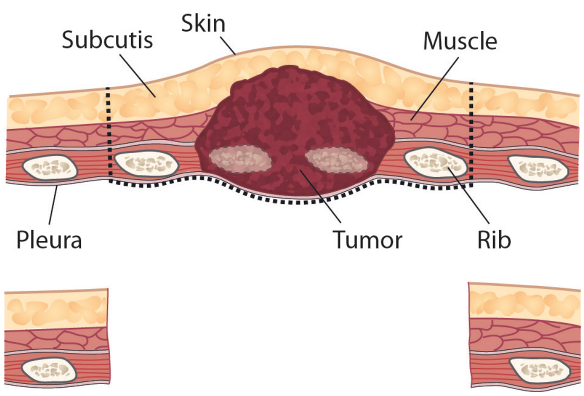

Figure 11. Full-thickness chest wall resection (all layers).

2.6.2 Diaphragm resection

An isolated diaphragm resection is seldom performed for oncological reasons, because the primary or secondary tumour rarely grows in the diaphgram (Baldes, Schirren 2016). Typically, a diaphragm resection and reconstruction represents a part of the procedure in a thoracoabdominal wall tumour **(Figure 12)** resection (Mansour, Thourani et al. 2002) or in an extrapleural pneumonectomy or pleurectomy decortication due to mesothelioma (Bassuner, Rice et al. 2017). The diaphragm separates the thoracic and abdominal cavity, providing a natural border between these two structures and helping to achieve wide margins in an oncological resection surgery (Tukiainen 2013).

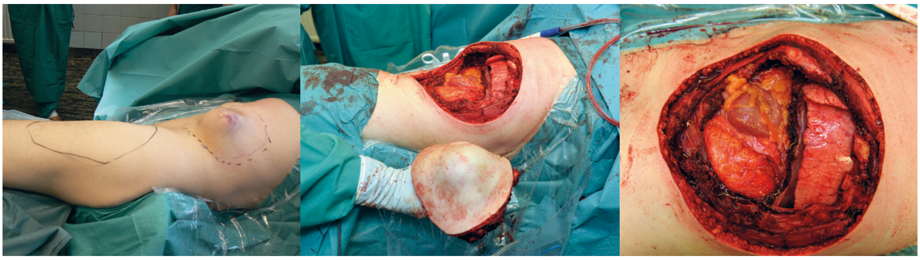

Figure 12. (Left) Thoracoabdominal wall sarcoma. (Middle and right) Full-thickness thoracoabdominal wall and partial diaphragm resection.

2.7 Reconstruction of the chest wall

2.7.1 The goals of chest wall reconstruction

Chest wall reconstruction aims to maintain adequate respiratory functioning, avoid lung herniation, protect vital intrathoracic organs, create a stable platform to support the shoulders and upper extremities and achieve an airtight closure (Tukiainen 2013, Mahabir, Butler 2011, Althubaiti, Butler 2014, Thomas, Brouchet 2010). Reconstruction should also achieve adequate stability allowing for physiological movements and obliterate any dead space in the chest wall cavity (Bakri, Mardini et al. 2011, Netscher, Baumholtz 2009, Harati, Kolbenschlag et al. 2015).

Soft-tissue flap coverage is an important part of reconstruction not only in order to achieve the aims of reconstruction (Althubaiti, Butler 2014, Arnold, Losken, Thourani et al. 2004), but also to achieve an acceptable cosmetic result (Tukiainen 2013).

2.7.2 General principles of chest wall reconstruction and stabilisation

Extensive chest wall resection and reconstruction pose a significant challenge to surgeons, which is also potentially life-threatening to the patient. Thus, a careful multidisciplinary approach in patient selection and treatment, as well as during perioperative and postoperative therapy, is essential to achieving the optimal and earliest possible recovery. The timing of surgery and treatment should be individually determined. Planning should be carefully carried out in order to achieve a fast and safe operation (Tukiainen 2013).

Chest wall defects can be either full or partial thickness. Reconstruction carries two characteristics: stabilisation and soft-tissue reconstruction or coverage. Whether chest wall skeletal support restoration is mandatory for stabilisation remains contested, and largely depends on the size of the defect. Reports indicate that, in large chest wall defects, mesh reconstruction reduced ventilator dependence and hospital stays in comparison to reconstruction without mesh (Kroll, Walsh et al. 1993).

In small defects, consisting of one or two ribs, some surgeons use a synthetic mesh to prevent bulging or herniation of the lung (Mansour, Thourani et al. 2002, Tukiainen 2013). Defects larger than 5 cm or extending over four ribs require stabilisation with mesh or with another stabilisation method (Harati, Kolbenschlag et al. 2015, Netscher, Baumholtz 2009).

The location of the defect is also an important factor in evaluating the need for chest wall stabilisation. Stabilisation of the posterior chest wall is less often required given that the scapula bone supports the posterior chest wall (Deschamps, Tirnaksiz et al. 1999, Losken, Thourani et al. 2004). Accordingly, Mansour et al. argue that soft-tissue reconstruction is only adequate for posterior chest wall defects under the scapula above the fourth rib (Mansour, Thourani et al. 2002).

Semirigid stabilisation is achieved through the use of a bioprosthetic matrix or synthetic mesh **(Figure 13)** (Althubaiti, Butler 2014). Specifically, for large or extensive anterior or anterior-lateral defects, more rigid stabilisation can be achieved using techniques such as the sandwich method technique (methylmethacrylate sandwiched between two layers of mesh; **Figure 14)** (Lardinois, Muller et al. 2000), a rib graft with mesh, titanium plates (Berthet, Canaud et al. 2011) and titanium mesh (Tamburini, Grossi et al. 2019, Yang, H., Tantai et al. 2015). A history of radiation to the defect area impacts the stability of the chest wall. Radiation fibrous provides more stability, diminishing the need for chest wall stabilisation with mesh in some cases (Losken, Thourani et al. 2004). In large full-thickness chest wall defects, stabilisation combined with soft-tissue reconstruction is necessary **(Figure 14).**

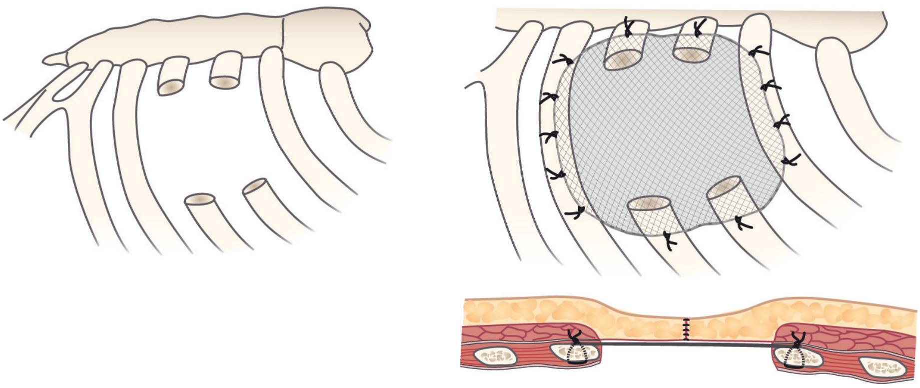

Figure 13. Partial-thickness resection and chest wall stabilisation with mesh.

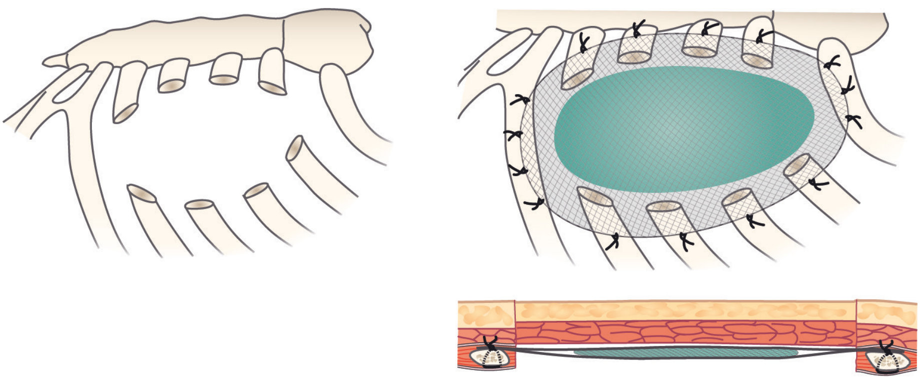

Figure 14. Full-thickness chest wall resection and chest wall stabilisation using the sandwich technique and soft-tissue reconstruction with a flap.

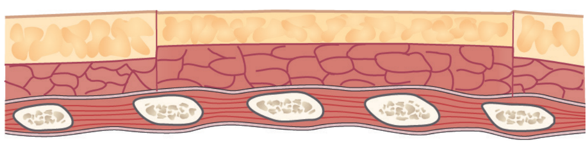

Figure 15. Partial-thickness resection (soft tissue) and soft-tissue reconstruction with a flap.

The size and location of the chest wall defect, the availability of local and pedicled flaps, previous operations or radiotherapy and the general condition and prognosis of the patient all impact the choice of soft-tissue flap reconstruction. The first choice is typically the pedicled myocutaneus flap. If the flaps are inadequate in terms of the dimensions or otherwise unavailable, the second choice is the microvascular free flap (Arnold, Pairolero 1996, Tukiainen 2013).

Following chest wall stabilisation in skeletal bony defects, soft-tissue flap reconstruction is not obligatory if the primary closure can be achieved using healthy, well-vascularised soft tissue. In partial-thickness soft-tissue defects, a soft-tissue flap reconstruction is adequate **(Figure 15).** Skin graft is rarely used given that it is unable to cover exposed bone, cartilage or prosthesis (Tukiainen 2013).

2.7.3 Chest wall stabilisation

The introduction of synthetic mesh replaced autologous stabilisation methods (Arnold, Pairolero 1996). The benefits of these alloplastic prosthetics include no donor-specific morbidity, a limitless availability and no harvesting time needed for a graft (Mahabir, Butler 2011). In the 1980s, le Roux and Shama defined the characteristics of an ideal synthetic material for stabilisation: inexpensive, physically and chemically inert, sterilisable, malleable, resistant to infection, radiolucent, rigidity eliminating paradoxical movements and allowing the ingrowth of fibrous tissue (le Roux, Shama 1983). Unfortunately, at present, no ideal material is available (Khullar, Fernandez 2017, Mahabir, Butler 2011) and the choice of prosthetic material normally depends on the surgeon's preference and experience, as well as characteristics of the defect (Arnold, Pairolero 1996, Khullar, Fernandez 2017, Mahabir, Butler 2011).

Technically, all stabilisation materials (autologous or alloplastic) should be sutured under tension to fill the defect (Mahabir, Butler 2011).

2.7.3.1 Autologous

Various autologous reconstruction materials have been used to stabilise the chest wall. In the past, the most common autologous reconstructions consisted of bone or fascial grafts (Althubaiti, Butler 2014). In the late 1940s, fascia lata (Watson, James 1947) and avascular rib grafts (Bisgard, Swenson 1948) were described. In the late 1950s, Brodin et al. introduced chest wall stabilisation using the iliac crest (Brodin, Linden 1959). Autologous stabilisation methods carry several disadvantages. For example, donor-specific morbidity and a limited amount of graft for larger defects represent disadvantages of bone grafts (Althubaiti, Butler 2014). Furthermore, the fascia lata can become too flaccid to resolve in the long term (Tukiainen 2013). Indeed, in a contaminated abdominal wall reconstruction, the avascular fascia lata serves as a reliable adjuvant for stabilisation (Disa, Goldberg et al. 1998). A tensor fascia lata muscle (TFL) flap and an anterolateral (ALT) flap can be combined with a fascia lata and a vascularised fascia can be used in chest wall stabilisation (Tukiainen 2013).

2.7.3.2 Alloplastic

2.7.3.2.1 Synthetic meshes

At present, several synthetic meshes are available with varying properties and thicknesses. **Table 3** summarises commonly used meshes in chest wall stabilisation. None have proven better than others and the choice of mesh typically stems from the surgeon's preference and experience (Seder, Rocco 2016, Mahabir, Butler 2011, Khullar, Fernandez 2017).

Table 3. Synthetic meshes used for chest wall stabilisation.

Material	Publication	Trademark of mesh
Polypropylene (PP)	(Mansour, Thourani et al. 2002, Kroll, Walsh et al. 1993, Chang, Mehrara et al. 2004, Weyant, Bains et al. 2006)	Marlex (CR Bard, Murray Hill, NJ, USA)
	(Deschamps, Tirnaksiz et al. 1999, Mansour, Thourani et al. 2002, Salo, Tukiainen 2018, Arnold, Pairolero 1996)	Prolene (Ethicon, Inc, Somerville, NJ, USA)
	(Salo, Tukiainen 2018)	Parietex (Medtronic, Minneapolis, MN, USA)
Polytetrafluoro-ethylene (PTFE)	(Deschamps, Tirnaksiz et al. 1999, Weyant, Bains et al. 2006, Arnold, Pairolero 1996)	Gore-Tex patch (W.L. Gore & Associates, Inc, Flagstaff, AZ, USA)
	(Nagayasu, Yamasaki et al. 2010)	Dualmesh (W.L. Gore & Associates, Inc, Flagstaff, AZ, USA)
	(Azoury, Grimm et al. 2016, Leuzzi, Nachira et al. 2015)	NR
Polyester	(Belmahi, Ouezzani et al. 2007, Abbes, Mateu et al. 1991)	Mersilene (Ethicon, Inc, Somerville, NJ, USA)
Polyglycolic acid	(Omote, Ikeda et al. 1994)	Dexon (Sherwood, Davis & Geck, St Louis, MO, USA)
Polydioxane	(Puma, Ragusa et al. 1992)	PDS (Ethicon, Somerville, NJ, USA)
Polyglactin	(Mansour, Thourani et al. 2002, Leuzzi, Nachira et al. 2015)	Vicryl (Ethicon, Inc, Somerville, NJ, USA)
Nylon	(Eschapasse, Gaillard et al. 1981)	NR
Titanium mesh	(Yang, H., Tantai et al. 2015)	Timesh/Flexmesh (Medtronic Neurologic Technologies)
	(Tamburini, Grossi et al. 2019)	MDF (Medica S.r.l, Italy)
Polymethyl meth-acrylate (PMMA) Methylmeth-acrylate (MMA) (Sandwich technique)	(Mansour, Thourani et al. 2002, Chang, Mehrara et al. 2004, Azoury, Grimm et al. 2016, Weyant, Bains et al. 2006, Salo, Tukiainen 2018, Lardinois, Muller et al. 2000, Khalil, Malahias et al. 2016	

NR, not reported.

2.7.3.2.2 Bioprosthetic materials (biological mesh, acellular dermal matrix)

The first report of chest wall reconstructions using an acellular dermal matrix (ADM) appeared in 2004 (Cothren, Gallego et al. 2004).

In recent years, more than ten different bioprosthetic meshes are used in surgery. These biological meshes are classified according to the source material: allograft (human cadaveric source) and xenogaft (porcine or bovine source). Most products consist of decellularised tissue material containing collagen elastin, fibrillin and glycosaminoglycans (Sodha, Azoury et al. 2012). The benefits of these matrix products include revascularisation, cellular infiltration and remodeling into autologous tissue after implantation (Mahabir, Butler 2011, Khullar, Fernandez 2017).

In the last decade, chest wall reconstruction using ADM has become more popular (**Table 4)** (Miller, Force et al. 2013, Khalil, Kalkat et al. 2018, Azoury, Grimm et al. 2016, Lin, Kastenberg et al. 2012, Barua, Catton et al. 2012, D'Amico, Manfredi et al. 2018, Ge, Imai et al. 2010, Giordano, Garvey et al. 2020). However, the role of ADM materials in chest wall reconstruction has not been clearly defined. In early ADM studies, the number of patients has remained rather limitied with a short follow-up time.

Recently, Giardano et al. (2020) published the first retrospective study comparing ADM and synthetic mesh in chest wall reconstructions. They reported fewer surgical site complications ($p = 0.027$) in the ADM reconstruction group (16%) than in the synthetic mesh group (33%). Their study included 146 patients (95 receiving synthetic mesh and 51 receiving ADM), with a mean defect size area reaching 174 cm^2. The mean follow-up period was 29 months (Giordano, Garvey et al. 2020).

Table 4. Bioprosthetic materials used in chest wall reconstruction.

Material	Publication	Trademark	
Bovine pericardium	(Miller, Force et al. 2013, Barua, Catton et al. 2012)	Veritas	Synovis Life Technologies Inc, St Paul, MN, USA
Porcine dermis	(Khalil, Kalkat et al. 2018, Giordano, Garvey et al. 2020)	Strattice	Allergan, Irvine, CA, USA
Porcine dermis	(Lin, Kastenberg et al. 2012, Barua, Catton et al. 2012)	Permacol	Covidien, Mansfield, MA,USA
Porcine dermis	(D'Amico, Manfredi et al. 2018)	Protexa	Tecnoss, Gaiveno, Italy
Bovine dermis	(Giordano, Garvey et al. 2020)	SurgiMend	TEI Biosciences, Inc., Boston, MA, USA
Porcine small intestine mucosa	(Smith, Campbell 2006)	Surgisis	Cook Biomedical, Bloomington, IN, USA
Cadaveric human dermis	(Ge, Imai et al. 2010, Butler, Langstein et al. 2005, Giordano, Garvey et al. 2020)	AlloDerm Alloderm FlexHD	Allergan, Irvine, CA, USA LifeCell Corp, Branchburg, NJ, USA Musculoskeletal Transplant Foundation, Edison, NJ, USA
NR	(Azoury, Grimm et al. 2016)	NR	

NR, not reported

2.7.3.2.3 Sandwich technique

In anterior or anterolateral large chest wall defects, a material more rigid than mesh is favoured for stabilisation. In 1981, McCormack et al. introduced the sandwich technique, where methylmethacrylate (MMA) or polymethylmethacrylate (PMMA) is sandwiched between two layers of marlex mesh (McCormack, Bains et al. 1981).

The sandwich technique (**Figure 12,** page 34) relies on two meshes shaped slightly larger than the defect. Then, MMA or PMMA is added between two layers of mesh, thereby creating a sandwich. The thin MMA or PMMA plate should be smaller than the bony defect. The meshes of the sandwich are sutured to the defect edges (Mahabir, Butler 2011, Tukiainen 2013).

The sandwich technique carries several advantages. First, it offers a more rigid reconstruction than mesh, and is a fast technique, suc that the construct is perioperative customised based on the shape and size of the chest wall defect (Chang, Mehrara et al. 2004, Lardinois, Muller et al. 2000, Tukiainen 2013, Mansour, Thourani et al. 2002).

A recent meta-analysis of the sandwich technique included 75 studies, finding a complication rate reaching 13.7%. The most common complications included infection (5.6%), respiratory failure (3.3%) and atelectasis (1.7%). The overall mortality rate due to respiratory problems was 1.6% (Shah, Ayyala et al. 2019). In addition, Weyant et al. reported an increased wound complication rate following the MMA sandwich technique. The wound infection rate in their series reached 5.3% (Weyant, Bains et al. 2006).

2.7.3.2.4 Plates and osteosynthesis systems

Over time, surgeons have performed surgical fixation of multiple rib fractures to avoid a flail chest and respiratory insufficiency (Beks, Peek et al. 2019). At the beginning of the twenty-first century, the first titanium plates, bars and screws for rib fracture fixation were introduced. Using this method, a plate is afixed to the ribs with a hook (Moreno De La Santa Barajas, P, Polo Otero et al. 2010). In the last decade, these osteosynthesis materials were introduced for chest wall stabilisation after chest wall resection as well. These rigid implants aim to maintain the curved shape of the chest wall and prevent volume depletion in the chest cavity (Berthet, Canaud et al. 2011). In the literature, the three different fixation systems shown in **Table 5** have gained some popularity. The results from using this osteosynthesis system in chest wall reconstruction remain controversial. Some studies report good outcomes with minimal plate-related morbidity, although the number of patients is rather small. Some patients experienced trauma with rib fractures, and the median follow-up was at best 20 months (De Palma, Sollitto et al. 2016, Bille, Okiror et al. 2012, Iarussi, Pardolesi et al. 2010).

Berthet et al. (Berthet, Canaud et al. 2011) also published solid results (with an early implant failure rate of 13%) using titanium plates and a dual mesh in large chest wall reconstruction (n = 19) following tumour resection. In 2015, the same group published another article concerning osteosynthesis following tumour resection patients (n = 29) and chest wall deformity patients (n = 25). In a long-term follow-up study, they noticed a higher rate of implant failures (broken or displaced), reaching as high as 44% (Berthet, Gomez Caro et al. 2015).

Table 5. Plates and osteosynthesis systems in chest wall reconstruction.

Material	Publication	Trademark	
Titanium	(Khalil, Malahias et al. 2016, Bille, Okiror et al. 2012, Berthet, Canaud et al. 2011)	Stratos	MedXpert, Heitersheim, Germany
Titanium	(Ng, Ho et al. 2014, De Palma, Sollitto et al. 2016)	MatrixRIB fixation	Depuy Synthes, West Chester, PA, USA
Titanium	(Bille, Okiror et al. 2012, De Palma, Sollitto et al. 2016, Iarussi, Pardolesi et al. 2010)	Sternal fixation system	Synthes, Solothurn, Switzerland

2.7.4 Chest wall soft-tissue reconstruction

A soft-tissue flap reconstruction is based on the size and location of the chest wall defect, the availability of local and pedicled flaps, previous operations or radiotherapy and the general condition and prognosis of the patient. When local or pedicled flaps are inadequate in size or dimension or are unavailable, a microvascular free-flap reconstruction may be necessary (Tukiainen, Popov et al. 2003). When selecting the flap, the surgeon should understand that closing the flap donor site will not increase the defect size in the reconstruction area and the donor site of the flap should not negatively impact breathing (Arya, Chow et al. 2016).

Pedicled myocutaneous flaps are the first choice for soft-tissue reconstruction of the chest wall (Arnold, Pairolero 1996). The most commonly used flap reconstruction is the ipsilateral musculocutaeous latissimus dorsi, considered the workhorse flap by many. This type of flap can provide rather large flap coverage and the dorsolateral donor site is closed primarily or with a skin graft if primary closure is impossible. The pectoralis major and rectus abdominis muscle flaps derive from other pedicle muscles, which can be used if the defect size and location are suitable. All of these muscle flaps are reliable and robust, feature a constant vascular anatomy and arch or rotation can result in musculocutaneus flap harvest (Bakri, Mardini et al. 2011).

Patients with primary extremity soft-tissue sarcomas undergoing neoadjuvant RT present with independent risk factors for wound complications (Dadras, Koepp et al. 2020). In addition, in the chest wall area, the previous RT area should be taken into account when planning the flap harvesting area to avoid flap-related problems and donor site problems (Tukiainen 2013).

2.7.4.1 Local or pedicled flaps

2.7.4.1.1 Latissimus dorsi muscle flap

The latissimus dorsi muscle or latissimus dorsi musculocutaneous **(Figure 16)** flap has been used as a workhorse flap in several surgical series for chest wall reconstructions (Mansour, Thourani et al. 2002, Chang, Mehrara et al. 2004, Deschamps, Tirnaksiz et al. 1999, Arnold, Pairolero 1996). Given the large volume of the latissimus dorsi muscle flap, it is commonly used to eliminate dead space accompanying intrathoracic defects (Chen, Bonneau et al. 2016, Arnold, Pairolero 1989) since damage to the muscle should be avoided during routine thoracotomy.

The latissimus dorsi flap carries multiple strengths. These include a large size and volume and tailoring the flap to the defect, whilst the relatively long pedicle allows a wide arc of rotation and easy harvesting. The skin island of the cutaneous flap can only be harvested to a width of 7 to 10 cm if the donor site is closed directly. The shape and location of the skin island in a musculocutaneous latissimus dorsi flap can be transformed, assisting reconstruction and specifically closing the skin defect (Bakri, Mardini et al. 2011). When a large skin island is harvested, the donor area must be skin grafted. The flap can be used to cover most anterior, anterior-lateral and posterior-lateral defects.

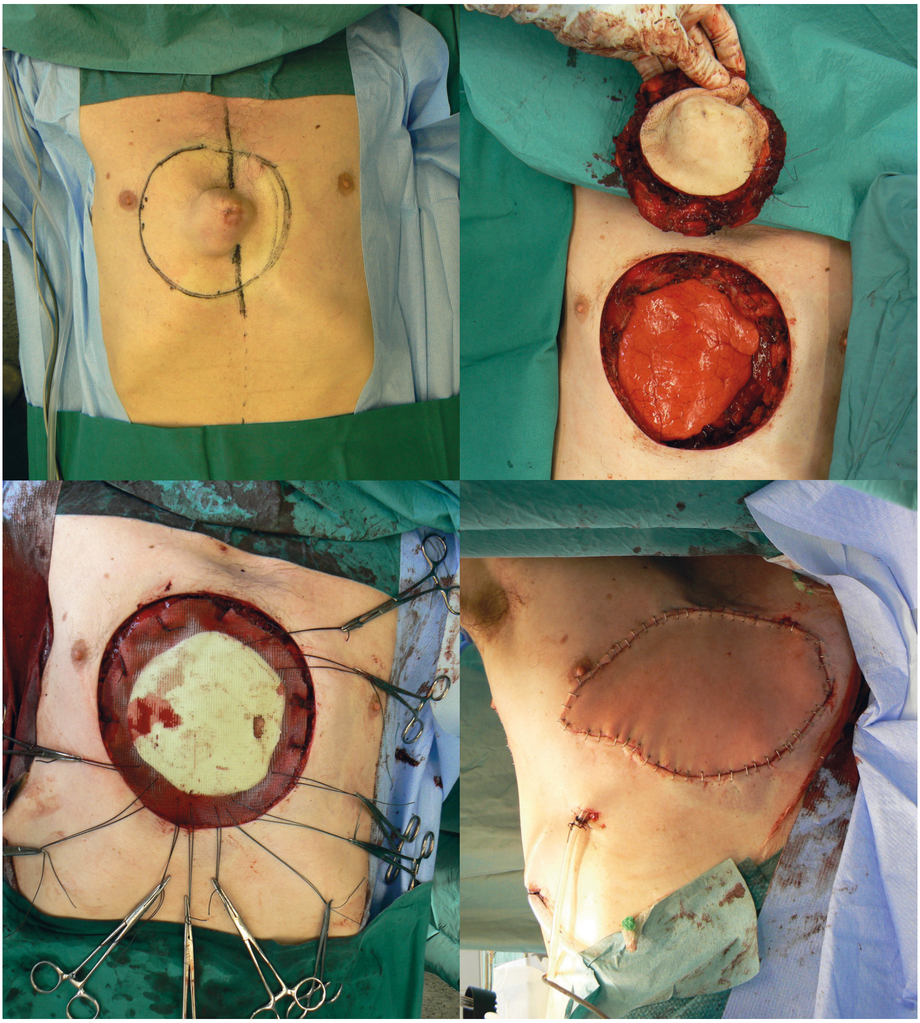

Figure 16. (Above, left) Chest wall chondrosarcoma. (Above, right) Full-thickness anterior chest wall resection. (Below, left) Chest wall stabilisation with a methylmethacrylate sandwich technique (between two meshes). (Below, right) Soft-tissue reconstruction with a pedicled musculocutaneus latissimus dorsi flap.

2.7.4.1.2 Rectus abdominis muscle flap and musculocutaneous alternatives

A pedicled rectus abdominis muscle flap (Chang, Mehrara et al. 2004, Weyant, Bains et al. 2006) or various musculocutaneous alternatives (i.e., transversal rectus abdominis, TRAM; vertical rectus abdominis muscle, VRAM) are options to cover anterior, anterior-lateral chest and thoracoabdominal wall defects. The rectus abdominis muscle is sourced from the superior epigastric and the deep inferior epigastric artery, which are both dominant pedicles. In the reconstruction of chest wall defects, a pedicled flap is established on the superior epigastric pedicle. A VRAM flap design is quite appropriate for long vertical anterior defects, whereas a TRAM flap can be harvested as a wider transversal skin paddle without any primary closure issues. As an extra advantage, this resembles an aesthetic abdominoplasty.

Using a rectus abdominis muscle flap is associated with donor-site morbidity, specifically the risk of an abdominal wall hernia. Harvesting the flap could also affect the early and postoperative dynamics of breathing. Damage to the ipsilateral internal mammary vessels does not preclude using a rectus abdominis muscle flap, since the superior epigastric pedicle could still be vascularised through the lower intercostal and musculophrenic artery (Netscher, Eladoumikdachi et al. 2001). Musculocutaneous rectus abdominis flaps may develop venous congestion following ligation of the deep inferior epigastric pedicle. The flap could be supercharged via vein anastomosis for these types of venous problems (Cordeiro, Santamaria et al. 2001).

2.7.4.1.3 Pectoralis major muscle flap

The pectoralis major muscle flap is a popular choice for chest wall reconstruction (Arnold, Pairolero 1996, Azoury, Grimm et al. 2016, Deschamps, Tirnaksiz et al. 1999). The vascularity of the flap relies on a dominant thoracoacromial pedicle and secondary intramammary pedicles. The flap can be used as a pedicle flap supplied from the throcoacromial vascular pedicle. When the flap is based on the secondary pedicles, it can be used as a split turnover flap. This flap can best reach the anterior chest wall, and can also be harvested with a skin island. It is also possible to use bilateral flaps for larger defects. A pectoralis major flap is classically used as a workhorse in reconstruction following sternotomy infection (Arnold, Pairolero 1996, Izaddoost, Withers 2012).

2.7.4.1.4 External oblique muscle flap

The external oblique muscle is located in the abdominal wall, from which a flap is also used for chest wall reconstruction. The use of this flap, however, has not become as common as the latissimus dorsi, pectoralis major or rectus abdominis muscle flaps. In the 1990s, several surgeons (Arnold, Pairolero 1996) used this flap in chest wall reconstructions. More recently, Chang et al. have continued using this flap (Chang, Mehrara et al. 2004). Lee et al. recently published results from a study of 75 reconstructions following advanced or recurrent breast cancer. They reported low complication rates and short (under two hours) operating times (Lee, Jung et al. 2018). This flap can be used for thoracoabdominal and anterior-lateral reconstructions.

2.7.4.1.5 Serratus anterior muscle flap

The serratus anterior muscle flap is typically used together with other flaps supplied from the subscapular vascular system, including latissimus dorsi, scapular and parascapular flaps. Ordinarily, these chimeric flaps, including the serratus anterior flap, are harvested for the reconstruction of extensive chest wall defects (Althubaiti, Butler 2014). In select cases, the serratus anterior muscle can be used on its own in anterior-lateral and posterior-lateral chest wall reconstructions (Arnold, Pairolero et al. 1984).

2.7.4.2 Pedicled perforator flaps

2.7.4.2.1 Intercostal artery perforator (ICAP) flap

The intercostal artery perforator (ICAP) flap and the thoracodorsal artery perforator (TDAP) flap are the most commonly used perforator flaps for a chest wall reconstruction, although other perforator flaps have also been described in the literature. These include the superior epigastric artery perforator, internal mammary artery perforator, lateral thoracic artery perforator and dorsal scapular artery perforator flaps (Florczak, Chaput et al. 2018).

The ICAP flap is based on anterior, lateral or posterior intercostal artery perforators. Jian et al. successfully harvested and used a lateral ICAP flap to reconstruct defects of the axilla area due to lymphatic malformations (Jiang, Li et al. 2014). Likewise, Yu et al. reported using an anterior ICAP flap to cover a chest wall defect after a dermatofibrosarcoma resection (Yu, Zang et al. 2016).

The thoracoepigastric transposition flap, typically supplied by the perforator from the epigastric arcade or intercostal arteries, represents a modification of the perforator flap. Thoracoepigastric flaps can cover smaller defects in the lower part of the chest wall or in the thoracoabdominal area (Harati, Kolbenschlag et al. 2015).

2.7.4.2.2 Thoracodorsal artery perforator (TDAP) flap

TDAP flaps based on the thoracodorsal artery perforator are used to cover moderately sized defects on anterior, anterior-lateral and posterior-lateral chest wall defects. Yang et al. reported an excellent survival rate for these flaps (100%) with a low donor-site morbidity (Yang, L. C., Wang et al. 2013).

2.7.4.2.3 Superior epigastric artery perforator (SEAP) flap

The superior epigastric artery perforator (SEAP) flap can cover anterior chest wall defects and has been used in reconstructions following sternotomy infection

(Wettstein, Weisser et al. 2014, Eburdery, Grolleau et al. 2016). The main benefit of the SEAP flap lies in the relatively short operation time (Wettstein, Weisser et al. 2014) and its sparing of the rectus abdominis muscle (Eburdery, Grolleau et al. 2016).

2.7.4.3 Others

2.7.4.3.1 Reverse abdominoplasty

In select reconstruction cases, a reverse abdominoplasty has been used to cover caudal or thoracoabdominal chest wall defects (Bury, Reece et al. 1995, Pantelides, Mondal et al. 2013). Notably, Pantelides et al. do not recommend the reverse abdominoplasty as the first choice for chest wall reconstructions. Instead, this method should only be used in specific cases as an alternative option to the pedicled or free-flap reconstruction (Pantelides, Mondal et al. 2013).

2.7.4.3.2 Omentum flap

The blood supply for an omentum flap relies on the left or right gastroepiploic artery. Typically, the right artery is preferred given its larger caliber and the need to supply a majority of the omental blood supply (Matros, Disa 2011). An omentum flap serves as an alternative choice for anterior and anterior-lateral reconstructions of chest wall defects (Hultman, Culbertson et al. 2001). This type of flap can be harvested laparoscopically (Pechetov, Esakov et al. 2017) or traditional open laparotomy (Jurkiewicz, Arnold 1977), and offers some advantages, including a large surface area and a long pedicle. However, the flap has to be skin grafted or covered with another flap. In rare cases, a microvascular-free omentum flap is used as a salvage procedure (Sauerbier, Dittler et al. 2011).

2.7.4.3.3 Breast flap

In special circumstances, an anterior midline chest wall defect can be reconstructed using a breast flap (Marshall 1993, Tukiainen 2013). The breast flap is supplied from a lateral thoracic artery. The major advantage of this flap is the fast operation time, which might be relevant in a highly morbid elderly patient cohort (Tukiainen 2013). One disadvantage of a breast flap is the poor cosmetic result (Matros, Disa 2011).

2.7.4.4 Microvascular free flaps

The following represent indications for a microvascular free flap:

a. Pedicled flap options have been used or the pedicle of local flaps is damaged due to previous radiotherapy or a surgical procedure (Harati, Kolbenschlag et al. 2015).

b. Pedicled flaps do not reach the defect, such as defects to the epigastrium region and the thoracoabdominal area (Tukiainen 2013).
c. The single pedicle flap is inadequate in terms of volume or size to cover the chest wall defect (Netscher, Baumholtz 2009).

2.7.4.4.1 General principles of chest wall free-flap reconstruction

The ideal microvascular free flap for a chest wall reconstruction features a constant anatomy, a reliable and sufficiently large pedicle, rapid harvesting, minimal donor-site morbidity and allowing for a two-team approach (Tukiainen, Popov et al. 2003).

To achieve a safe and fast operation, free-flap reconstruction should be carefully planned (Tukiainen 2013). Using a two-team approach and keeping the patient in one position throughout surgery when possible, a shorter operation time can be achieved (Arya, Chow et al. 2016).

The recipient vessels for the free flap are typically chosen near the resection site, where healthy vessels are easily accessible. In cases where the typical recipient vessels are unavailable or the flap positioning is extremely impractical, an arterio-venous (A-V) loop remains a solid option for gaining in- and outflow to the flap. The saphenous loop **(Figure 17)** from the lower leg is used as the recipient vessel to achieve good blood flow to the flap and to relieve positioning of the flap in the thoracoabdominal region (Tukiainen, Popov et al. 2003). Engel et al. used an A-V loop between the cephalic vein–thoracoacromial artery (CTA) loop in chest wall reconstructions (Engel, Pelzer et al. 2007).

In larger chest wall reconstruction series, a free-flap reconstruction was indicated in 21% (Salo, Tukiainen 2018), 11% (Mansour, Thourani et al. 2002), 10% (Losken, Thourani et al. 2004) and 6% (Chang, Mehrara et al. 2004) of patients. In these series, the median chest wall defect size was only reported by Salo et al., reaching 156 cm^2 (Salo, Tukiainen 2018).

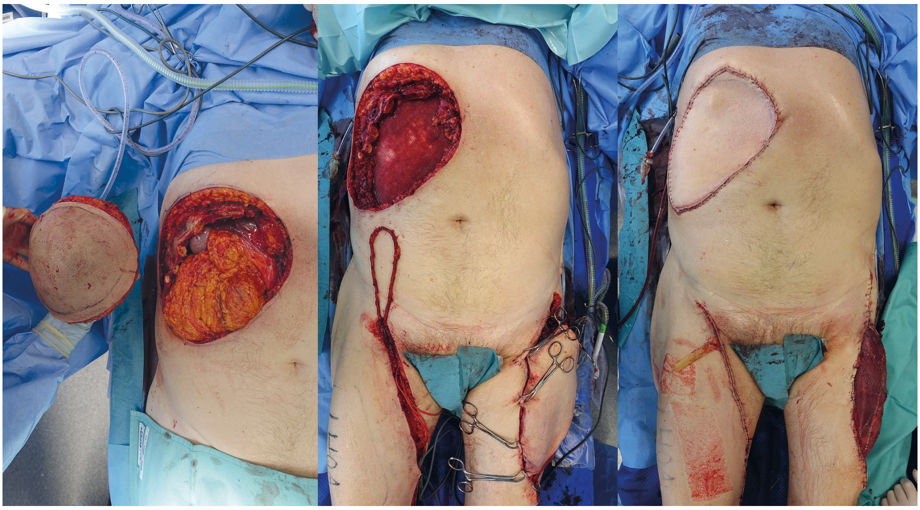

Figure 17. (Left) Full-thickness thoracoabdominal wall sarcoma resection. (Middle) Chest and abdominal wall reconstruction with mesh and a saphenous loop and a tensor fascia lata muscle (TFL) flap prepared. (Right) Soft-tissue reconstruction with a free TFL flap, with in- and outflow to the flap from the saphenous loop.

2.7.4.4.2 Flaps from the thigh

Tensor fascia lata (TFL) flap

Free flaps from the thigh rely on the descending branch of the arteria femoral profunda. These flaps are commonly used for chest wall or abdominal wall defects and carry several advantages. For instance, even a large donor site on the thigh does not impair breathing. In most cases, these flaps also allow for harvesting and reconstruction of the chest wall in the same position as the tumour resection, which can save time. Therefore, a two-team approach can be used. The tensor fascia lata (TFL) flap is a classic flap given the large flap size (up to 20 x 35 cm), whereby constant and large vessels permit safe anastomosis. Typically, the donor site must be covered with a skin graft if primary closure is impossible, although this is normally acceptable in this group of patients who have a malignant, large tumour removed. When a long and wide flap (**Figure 18**) is needed (including a skin island extending distally close to the knee), distal tip necrosis can develop in the flap. To overcome this, a muscle (vastus lateralis or rectus femoris) can be included in the flap. This normally yields extra perforators and vascularity to the distal part of the flap, whilst a donor-site defect is still acceptable (Tukiainen 2013).

Figure 18. (Left) Basal cell carcinoma (Gorlin-Goltz syndrome) of the chest wall. (Middle, left) Large resection of a tumour. (Middle, right). Soft-tissue reconstruction with an extended free thigh flap, rectus femoris combined with a TFL flap. (Right) Result two weeks postoperatively.

Anterolateral thigh (ALT) flap

In the twentieth century, the anterolateral thigh flap (ALT) served as a popular free soft-tissue reconstruction for a lower limb and the head and neck area (Wei, Jain et al. 2002). Currently, an ALT flap (**Figure 6,** page 28) is used more often in chest wall reconstructions (Di Candia, Wells et al. 2010, Song, Liu et al. 2019, Arya, Chow et al. 2016). The ALT flap has a long and good caliber pedicle (Di Candia, Wells et al. 2010), and a skin paddle flap can be harvested measuring 8 x 25 cm with direct closure (Sauerbier, Dittler et al. 2011).

2.7.4.4.3 Latissimus dorsi flap

The pedicled ipsilateral latissimus dorsi muscle flap is considered the workhorse flap for chest wall reconstructions, although repeated lateral thoracotomies can damage the pedicle of the flap and prevent the use of an ipsilateral flap. The contralateral latissimus dorsi muscle has been successfully harvested as a free flap (Cordeiro, Santamaria et al. 2001), but the position of the patient may require adjustment during surgery. This flap is reliable given the large diameter of the supplying thoracodorsal vessels. Moreover, the flap has a large volume, a long pedicle and donor-site morbidity remains minimal. In extensive defects, a latissimus dorsi flap can be used together with other flaps supplied from the subscapular vascular system, including parascapular and scapular flaps.

2.7.4.4.4 Rectus abdominis and musculocutaneous variants of rectus abdominis (TRAM and VRAM)

In the late twentieth century, the rectus abdominis muscle flap was popular in chest wall reconstructions as either a pedicled flap (Neale, Kreilein et al. 1981) or a free flap (Cordeiro, Santamaria et al. 2001), both of which carry poor donor-site morbidity rates. Flap harvesting commonly results in a donor-site defect of the anterior rectus muscle sheath. Despite careful reconstruction of the abdominal wall using a synthetic mesh, an abdominal wall hernia is possible (Sauerbier, Dittler et al. 2011).

Recently, Song et al. used musculocutaneous variants of a rectus abdominis muscle flap including TRAM, muscle-sparing TRAM and a vertical rectus abdominis muscle (VRAM) in a microvascular reconstruction of locally advanced breast cancer (Song, Liu et al. 2019). The advantages of the flap consist in its reliability, size and fast and easy harvesting (Tukiainen 2013).

2.7.4.4.5 Deep inferior epigastric perforator (DIEP) flap

The deep inferior epigastric perforator (DIEP) flap has been regarded as the gold standard in autologous breast reconstructions. Breast reconstruction surgeons are familiar with the DIEP flap, and have also used the DIEP flap in chest wall reconstructions. When the rectus muscle and function of the muscle is preserved, donor-site morbidity remains minimal (Arya, Chow et al. 2016). The DIEP flap can be harvested with a large dimension and can cover wide defects, although closing the donor site may increase the likelihood of an anterior chest wall defect (Tukiainen 2013). Furthermore, the surgical time may rise due to the intramuscular dissection of the pedicle of a DIEP flap (Sauerbier, Dittler et al. 2011).

2.7.4.4.6 Forearm fillet flap

The microvascular free forearm fillet flap represents a spare-part surgery used for the reconstruction of the chest wall following an extended forequarter amputation

(Cordeiro, Cohen et al. 1998). If the distal part of the arm or/and the forearm are tumour-free, a forearm fillet flap reconstruction can provide excellent coverage of an extended forequarter amputation area, whilst also providing a contour to the shoulder (Tukiainen 2013).

2.8 Reconstruction of the diaphragm

2.8.1 General principles

The diaphragm plays an important functional role in respiratory physiology and it separates the chest and abdominal cavities. Proper reconstruction of diaphragm defects is necessary in order to maintain the volume of the chest wall cavity, restore proper respiratory functioning and prevent herniation (Gaissert, Wilcox 2016). When performed as part of a thorcoabdominal wall resection, the diaphragm is normally resected distally, leaving the central areas and innervation intact. A too-tight primary closure results in a flat drum-head diaphragm with incomplete functioning (Bax, Collins 1984). Larger or complete resections of the diaphragm necessitate reconstruction with synthetic material or autologous tissues (Finley, Abu-Rustum et al. 2009).

2.8.2 Autologous and prosthetic material reconstruction of the diaphragm

A variety of flaps have been used for autologous diaphragm reconstruction, including the transversus abdominis and internal oblique muscles (Joshi, Sen et al. 2005), a combined flap reconstruction with omentum and latissimus dorsi flaps (Edington, Evans et al. 1989), a reversed latissimus dorsi flap (Bedini, Valente et al. 1997), a latissimus dorsi flap based on a primary pedicle (McConkey, Temple et al. 2006) and a TRAM flap (Hallock, Lutz 2004). The avascular fascia lata has also been used for diaphragm reconstruction (Kageyama, Suzuki et al. 1999, Yamashita, Asai et al. 2020).

Several types of synthetic materials have been used for diaphragm reconstruction, including synthetic meshes (**Figure 19**) (Finley, Abu-Rustum et al. 2009, Bassuner, Rice et al. 2017) and ADMs (Asai, Watanabe et al. 2011, Ricci, Higgins et al. 2014, Zardo, Zhang et al. 2011, Bassuner, Rice et al. 2017). Bassuner et al. compared polytetrafluoroethylene and an ADM in diaphragm reconstructions, finding that infection rates were similar in both groups. In addition, no statistically significant different herniation rates were observed. All reported herniations were acute, resulting from anchorage failure (Bassuner, Rice et al. 2017).

Figure 19. (Above, left) Full-thickness thoracoabdominal wall and partial diaphragm resection reconstructed using one mesh for the diaphragm and another mesh for the reconstruction of the thoracoabdominal wall. A tranverse suture line in the outer mesh indicates the original position of the diaphragm, where the other mesh was sutured. (Above, right) Large TFL flap harvested. (Below, left) Soft-tissue reconstruction using a TFL flap. (Below, right) Two weeks postoperatively.

2.9 Complications of chest wall surgery

The chest wall plays a crucially important anatomical and functional role. Complications resulting from chest wall reconstruction and reconstruction can be potentially life-threatening. In fact, postoperative 30-day mortality varies from 2.3% to 7%, with 90-day mortality ranging from 6.2% to 8.5% (**Table 6**).

During long surgeries which include several surgical sites, complications rather commonly occur despite advanced reconstruction techniques. Complications can be divided into general, surgical and respiratory complications. In the literature, we identified no randomised prospective trials comparing different reconstructive methods and prosthetic materials (Hazel, Weyant 2015). Thus, the complications and predictors of complications must be analysed using retrospective studies.

In such studies, complication rates vary from 16% to 46%. **Table 6** summarises the complication rates observed via large retrospective series. In an analysis of predictors of complications, the most significant factors consisted of defect size, patient age, concomitant lung resection, ulceration of the surgical area and the use of the omentum in the reconstruction (Lans, van der Pol et al. 2009, Weyant, Bains et al. 2006). Specifically, Giardano et al. reported in their comparative retrospective study of ADM and synthetic mesh in chest wall reconstructions finding fewer surgical site complications (p = 0.027) in ADM reconstructions (16%) than those accompanying synthetic mesh reconstructions (33%) (Giordano, Garvey et al. 2020). In another study, Corkum et al. reported that the resection of the superior or the middle ribs associated with an increased risk of pulmonary and general complications compared to inferior rib resections (p = 0.013) (Corkum, Garvey et al. 2020).

Table 6. Complications and mortality in chest wall resections and reconstructions.

Publication	Patients n	Complications %	30-day mortality %	90-day mortality %
(Corkum, Garvey et al. 2020)	59	26.6%	3.4%	8.5%
(Giordano, Garvey et al. 2020)	146	26.7%	NR	6.2%
(Lans, van der Pol et al. 2009)	220	34.0%	2.3%	NR
(Daigeler, Druecke et al. 2009)	92	42.4%	5.4%	NR
(Weyant, Bains et al. 2006)	262	33.2%	3.8%	NR
(Chang, Mehrara et al. 2004)	113	16.0%	4.0%	NR
(Mansour, Thourani et al. 2002)	200	24.0%	7.0%	NR
(Deschamps, Tirnaksiz et al. 1999)	197	46.2%	4.1%	NR

NR, not reported

2.10 Health-related quality of life

In recent decades, many cancer studies have included health-related quality-of-life (HRQofL) measurements as an endpoint (Bottomley, Aaronson et al. 2007). Until recently, information on long-term HRQoL following oncological chest wall resection and reconstruction has remained limited (Wakeam, Acuna et al. 2017). Assessing HRQoL can provide important information about treatment outcomes following chest wall resection and reconstruction.

In the literature, several different questionnaires have been used to estimate patient HRQoL. Commonly used instruments consist of the 15D (Sintonen 2001), the Short-Form 36 (SF-36) (Ware, Sherbourne 1992) and the EQ-5D (Brooks 1996). Furthermore, different tools such as the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire C30 QLQ-C30 questionnaire (Aaronson, Ahmedzai et al. 1993) and the Quality of Life for Cancer Survivors (QOL-CS) questionnaire (Ferrell, Dow et al. 1995) have been developed and validated for oncological patients.

Previous studies assessing HRQoL in patients following chest wall tumour resection all carry some limitations (Heuker, Lengele et al. 2011, Daigeler, Druecke et al. 2009, Liu, Wampfler et al. 2017, Nakao, Miyata et al. 1986, Tacconi, Ambrogi et al. 2012). For instance, they are hampered by small sample sizes (Daigeler, Druecke et al. 2009, Nakao, Miyata et al. 1986, Tacconi, Ambrogi et al. 2012, Heuker, Lengele et al. 2011) and do not compare results obtained in patients to findings amongst healthy controls (Tacconi, Ambrogi et al. 2012, Liu, Wampfler et al. 2017, Nakao, Miyata et al. 1986, Heuker, Lengele et al. 2011). Furthermore, such studies fail to report the extent of surgery, the need for reconstruction and the methods of reconstruction (Liu, Wampfler et al. 2017, Daigeler, Druecke et al. 2009). Moreover, no studies exist that assessed chest wall sarcoma patient HRQoL following surgery. Additionally, chest wall–related advanced breast cancer information on HRQoL following surgery remains limited (Wakeam, Acuna et al. 2017).

Previous studies have used pulmonary resection patients as the control group. Liu et al. observed no difference in HRQoL following chest wall resection for pulmonary resection compared to pulmonary resection without a chest wall resection (Liu, Wampfler et al. 2017). Yet, Daigeler et al. reported a significantly lower HRQoL following chest wall reconstruction compared to a healthy control group (Daigeler, Druecke et al. 2009). Moreover, Heuker et al. found that the subjective assessment of dyspnoea correlated well with patient-perceived HRQoL (Heuker, Lengele et al. 2011).

Tacconi et al. found that the extent of the chest wall resection, preoperative FEV1 and postoperative decline in the FVC served as the primary indicators for the decline in HRQoL measured by SF-36. The decline in HRQoL correlated with the extent of the surgical trauma (Tacconi, Ambrogi et al. 2012).

A meta-analysis of HRQoL results in chest wall resection patients treated for recurrent breast cancer was not feasible given reporting inconsistencies. One difficulty lies in that only 8 of 48 studies reported HRQoL. Amongst those eight, only one study validated the quantitative metrics used to report HRQoL (Wakeam, Acuna et al. 2017). In that study, the authors used the Union for International Cancer Control's (UICC) performance status, relying on data from only six patients. In that study, HRQoL improved due to the treatment (Nakao, Miyata et al. 1986).

2.11 Long-term survival following chest wall resection

Five-year survival following oncologic chest wall resection and reconstruction varied widely among different types of cancer.

Amongst advanced breast cancer patients, 5-year overall survival varied from 9% to 69% (Daigeler, Druecke et al. 2009, Petrella, Radice et al. 2016, Levy Faber, Fadel et al. 2013). Wakeam et al. in their meta-analysis (of 48 studies) reported an overall survival of 40.8% (Wakeam, Acuna et al. 2017).

In soft-tissue sarcoma studies, 5-year overall survival ranged from 45% to 89% (**Table 7**) (Gross, Younes et al. 2005, Pfannschmidt, Geisbusch et al. 2006, Tsukushi, Nishida et al. 2009, Soerensen, Raedkjaer et al. 2019, Nakahashi, Emori et al. 2019, McMillan, Sima et al. 2013). **Table 7** summarises 5-year disease-free survival (DFS) and local recurrence-free survival amongst soft-tissue sarcoma patients, as well as the prognostic factors for soft-tissue sarcoma.

Table 7. Overall survival, disease-free survival and local recurrence-free survival in soft-tissue sarcoma from chest wall resection studies.

Publication	Patients (n)	High-grade sarcoma, %	Follow-up time in months, median	5-year OS	5-year DFS	5-year LRFS	Negative prognostic factors for survival
(Soerensen, Raedkjaer et al. 2019)	88	87%	79	55%	NR	77%	high-grade tumour, intralesional/ marginal resection
(Nakahashi, Emori et al. 2019)	38	87%	NR	45%	27%	NR	tumour size >70.5 mm, R1/R2 resection
(Harati, Kolbenschlag et al. 2018)	110	42%	115	66%	NR	61%	age >50, tumour size >5 cm, angiosarcoma, grade III histology
(Oksuz, Ozdemir et al. 2014)	26	50%	82	69%	38%	62%	high-grade tumour
(McMillan, Sima et al. 2013)	192	57%	51	73%	NR	NR	NR
(Tsukushi, Nishida et al. 2009)	44	50%	57	89%	NR	89%	age >50, high-grade tumour, local recurrence
(Pfannschmidt, Geisbusch et al. 2006)	25	52%	47	57%	NR	NR	high-grade tumour
(Gross, Younes et al. 2005)	55	42%	52	87%	75%	NR	tumour size >5 cm, high-grade tumour

OS, overall survival; DFS, disease-free survival; LFRS, local recurrence-free survival; NR, not reported

In chondro- and bone sarcoma studies, 5-year overall survival varied from 64% to 92% (Burt, Fulton et al. 1992, Fong, Pairolero et al. 2004, Gao, Zhou et al. 2019), and from 21% to 61% in advanced lung cancer (Facciolo, Cardillo et al. 2001, Magdeleinat, Alifano et al. 2001, Doddoli, D'Journo et al. 2005).

2.12 Palliative surgery

Oncological chest wall resection and reconstruction can be performed with a curative or palliative intent **(Figure 20)** (Daigeler, Druecke et al. 2009). Despite modern developments in oncological treatments, some patients suffer malignant tumour–related pain, infection, bleeding, ulceration or paralysis of the upper extremity (Tukiainen 2013). These problems can lead to significant impacts on the patient's quality of life and even social isolation. Unfortunately, palliative care is an often overlooked indication for surgery for chest-related breast cancer recurrence patients, whereby patients are often sent for surgical consultation too late (Wakeam, Acuna et al. 2017).

Clinical experience and studies support the role of palliative surgery in select patients (Tukiainen 2013, Daigeler, Druecke et al. 2009). Still numerous challenges exist in palliative chest wall resection and reconstruction. Palliative operations may be complicated due to a previous surgery, radiation therapy or patient-related characteristics. These operations should be planned by a team of specialists from the medical and surgical disciplines. In addition, unacceptable morbidity and a compromised quality of life related to the surgery should be avoided. Each palliative operation should be tailored to the specific needs of the individual patient and the clinical situation (Beahm, Chang 2004).

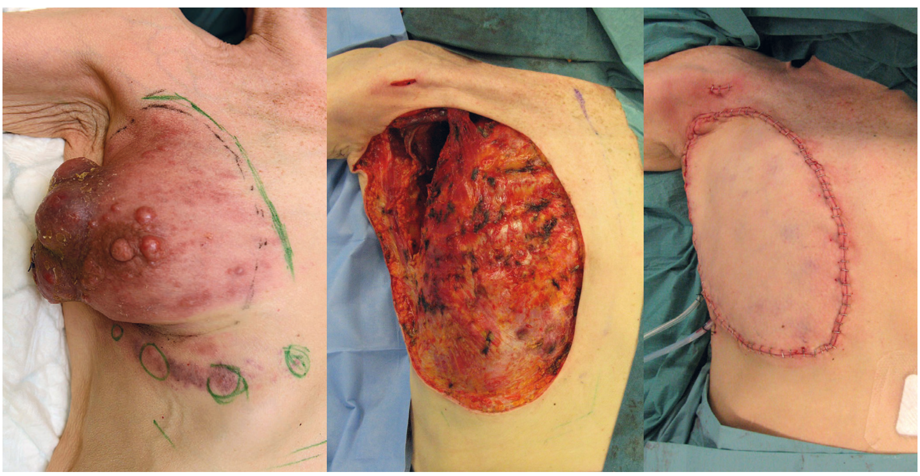

Figure 20. (Left) Metastatic breast cancer with a painful, bleeding and ulcerated large tumour. (Middle) Palliative partial-thickness chest wall resection. (Right) Soft-tissue reconstruction with a free TFL flap.

3 AIMS OF THE STUDY

This dissertation focuses on the following aims:

1. To analyse oncological resections and reconstructions of the chest wall with an emphasis on surgical outcomes and survival.

2. To describe and analyse our method for thoracoabdominal wall and diaphragm reconstruction.

3. To evaluate short-term outcomes, survival and tumour recurrence following chest wall resection amongst soft-tissue sarcoma patients and, further, to identify the independent prognostic factors for recurrence and survival. In addition, we aimed to analyse the benefits of adjuvant therapy in our patient series.
4. To assess the long-term HRQoL amongst patients following chest wall reconstruction after oncological resection.

4 PATIENTS AND METHODS

This study was conducted at Helsinki University Hospital, and patients were treated in the Department of Plastic Surgery at Töölö Hospital. The Institutional Review Board approved our study protocol.

4.1 Selection of the study population

We searched the hospital's electronic database and paper medical records to identify patients treated with a chest wall resection in the Department of Plastic Surgery in Helsinki, Finland, between 1 January 1997 through 31 December 2015. The Local Ethics Committee approved the research plan and study protocol. Throuh our search of the database, we selected 135 patients.

For inclusion in this study, we only selected patients who underwent oncological chest wall resection. We excluded patients based on the following criteria: a congenital chest wall deformity, chest wall infection such as an infected sternotomy, a benign tumour excision with direct closure, bronchopleural fistula or being under 17 years old.

The day of the chest wall surgery served as the beginning of the follow-up period, whilst the time of death or the end of the study period (30 June 2016), whichever occurred first, represented the end of the follow-up period.

Studies I and IV consisted of patients who underwent an oncological chest wall resection between January 1997 and December 2015**.**

Study II consisted of patients treated with a diaphragm and thoracoabdominal wall reconstruction between January 1997 and December 2015.

Study III consisted of patients surgically treated for chest wall soft-tissue sarcoma between January 1997 and December 2015.

4.2 Study design

In **study I,** we retrospectively examined 135 patients who underwent oncological chest wall resection during a 19-year period. **Study II** was a retrospective study of 21 patients who underwent a diaphragm reconstruction and thoracoabdominal wall reconstruction during a 19-year period. **Study III** was a retrospective analysis of 49 patients treated for primary soft-tissue sarcomas of the chest wall during a 19-year period. In **studies I through III,** we reviewed electronic and paper medical records to collect the following data: patient demographic characteristics;

tumour histopathology, margins and location; surgical details of the resection and reconstruction; possible pre- and postoperative radio- and chemotherapy; imaging studies; and complications. All sarcoma patients (**studies I–III**) were reviewed during a multidisciplinary sarcoma tumour board. **Study IV** was a cross-sectional study of 135 adult patients who underwent an oncological chest wall resection and reconstruction during a 19-year period. At the start of HRQoL data collection in February 2016, 55 (41%) of 135 surgical patients had died and 2 patients had moved overseas. We mailed two HRQoL questionnaires together with a questionnaire consisting of sociodemographic and clinical details to the remaining 78 patients. Patients were asked to sign an informed consent form if they were willing to participate in the study and to return the questionnaires via post in a prepaid envelope. If the patient did not reply within a three-week period, a reminder letter together with a new set of questionnaires was sent. In total, 55 patients (71%) completed the questionnaires. The HRQoL results for patients were compared to those from an age- and gender-standardised sample drawn from the general population (n = 1307) obtained from the Health 2011 Survey in the hospital catchment area (Koskinen S, Lundqvist A, Ristiluoma N (eds.)).

4.3 Definitions (studies I–IV)

The comorbidity burden was defined based on the Charlson comorbidity index (CCI), while complications relied on the Clavien–Dindo classification (CD). CCI (Charlson, Pompei et al. 1987) was calculated for each patient based on the diagnosis listed in the electronic medical records. We calculated a median index for all studies (studies I–IV).We used the CD classification (Dindo, Demartines et al. 2004) to categorise postoperative complications **(Table 8).** This classification relies on complication grades (I, II, IIIa, IIIb, Iva, IVb and V), determined by the severity and the type of therapy needed to correct the complication. Major complications are classified as CD grade IIIa or higher. The CD classification standardises the estimation of surgical complications reported in various surgical studies.

Table 8. Clavien–Dindo classification of surgical complications (Dindo, Demartines et al. 2004).

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including central nervous system complications)* requiring IC/ICU management
Grade IVa	Single-organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient
Suffix ‘d’	If the patient suffers from a complication at the time of discharge the suffix ‘d’ (for ‘disability’) is added to the respective grade of the complication. His label indicates the need for follow-up to fully evaluate the complication.

*Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks. CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

4.4 Surgical procedure (study II)

The diaphragm provides a natural barrier to achieving wide surgical resection margins if a malignant tumour is located on the thoracoabdominal wall just above or below the diaphragm **(Figure 21)**. After a radical *en-bloc* resection of the thoracoabdominal wall and diaphragm, reconstruction is necessary.

In reconstruction, it is important to consider maintaining a functional diaphragm dome **(Figure 22)**. Diaphragm reconstruction with mesh was required if the diaphragm resection extended beyond 3 to 4 cm since without mesh reconstruction the diaphragm cannot be pulled back to its normal location without too much tension.

Typically combined, a defect reconstruction begins with suturing the chest or abdominal wall stabilation mesh to the chest wall cranially. If diaphragm reconstruction is necessary, the other mesh is sutured to the defect of the diaphragm using 0-1/0 polypropylene or polyester sutures.

The diaphragm or diaphragm reconstruction mesh is then pulled to the original position laterally and sutured to the chest or abdominal wall mesh. The functional diaphragm dome is reconstructed. Then, the distal part of the chest or abdominal wall stabilation mesh is sutured to the muscular layers of the abdominal wall. Finally, the chest or abdominal wall soft-tissue defect are closed with a flap or directly.

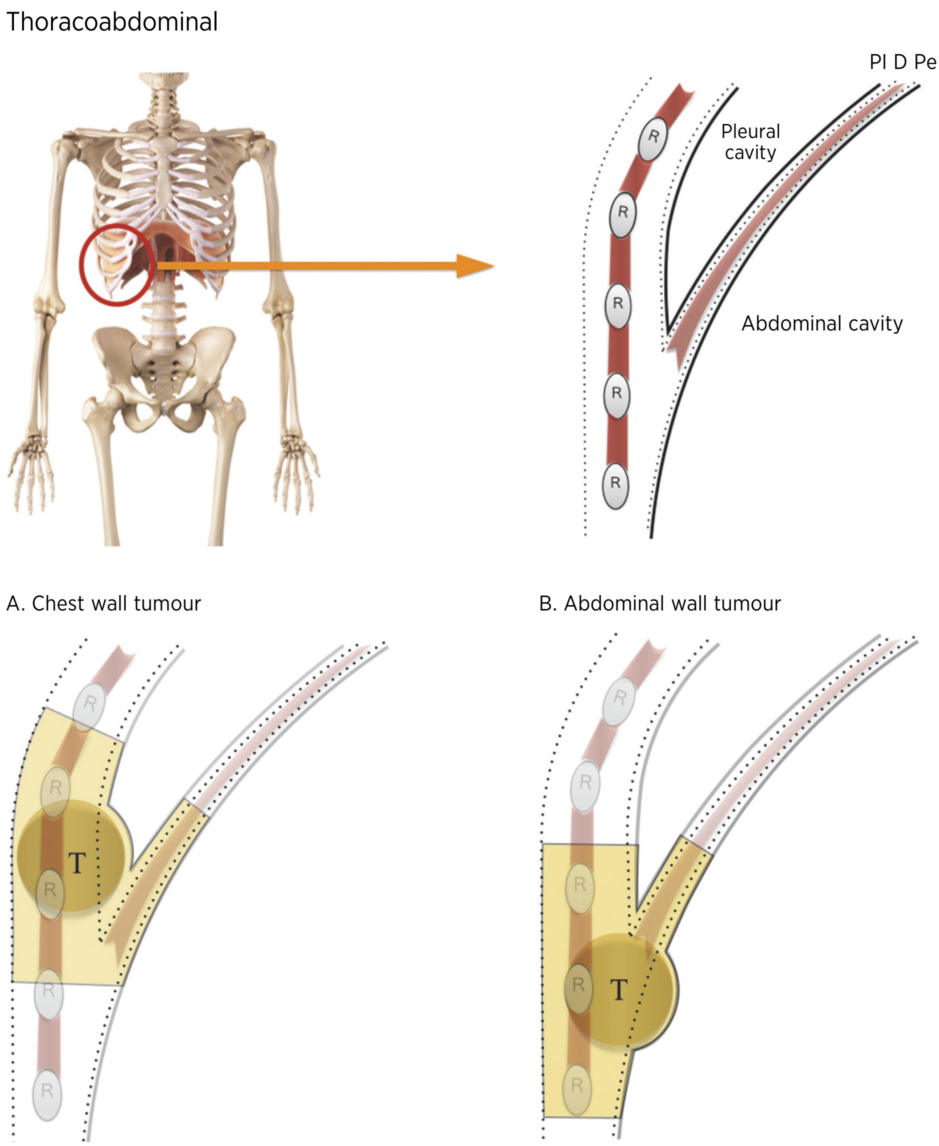

Figure 21. Thoracoabdominal wall tumour and resection technique.
R, rib; Pl, pleura; D, diaphragm; Pe, peritoneum; T, tumour.
(Reproduced with permission from the *Journal of Plastic Surgery and Hand Surgery* (Kuwahara, Salo et al. 2018).)

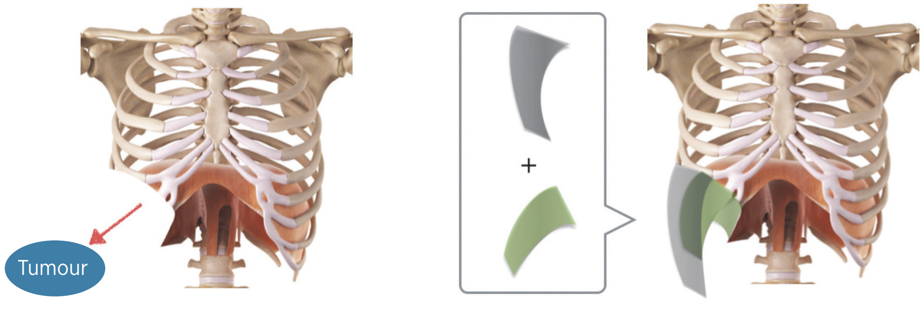

Figure 22. Thoracoabdominal wall resection and functional diaphragm dome reconstruction. (Reproduced with permission from the *Journal of Plastic Surgery and Hand Surgery* (Kuwahara, Salo et al. 2018).)

4.5 Oncological treatments (study III)

Patients were treated with neoadjuvant or adjuvant therapy if the surgical resection was marginal or/and the histology of the sarcoma was aggressive. Radiotherapy doses (conventionally fractionated) ranged from 42–66/1.5–2GY. Chemotherapy consisted of a doxorubicin (50 mg/m2) and ifosfamide (5 g/m2) combination (q21). Patients received four to six cycles. Granulocyte stimulating factor (G-CSF) was administered if the risk of infection was considered high or if a low white blood cell count caused a delay to treatment.

4.6 Health-related quality-of-life measurement instruments and forms (study IV)

4.6.1 The 15D questionnaire

Generic HRQoL was measured using 15D (Sintonen 2001), a comprehensive instrument that covers 15 dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental functioning, discomfort or symptoms, depression, distress, vitality, and sexual activities. Respondents rate each dimension on a scale from 1 (no problems) to 5 (severe problems). 15D produces both an HRQoL profile based on dimension-level values and a single index score representing overall HRQoL. Both are generated by incorporating the population-based preference weights onto the dimensions. The dimension-level values and the single index score fall on a 0 to 1 scale, where 0 represents being dead and 1 indicates the best possible HRQoL (15D score) or no problems on the dimension (dimension-level value). Estimates place the test–retest reliability and minimal clinically important difference of the 15D score at 0.90 and 0.015, respectively (Stavem 1999, Alanne, Roine et al. 2015). Furthermore, 15D compares favourably to other similar generic HRQoL instruments in their most important psychometric properties (Stavem 1999, Richardson, Iezzi et al. 2016, Sintonen 2001, Hawthorne, Richardson et al. 2001, Moock, Kohlmann 2008).

4.6.2 EORTC QLQ-C30 questionnaire

The EORTC Core Quality of Life questionnaire C30 (QLQ-C30) is a standardised and self-administered instrument designed for use in the estimation of HRQoL amongst oncological patients. QLQ–C30 incorporates nine multi-item scales including five functional scales, three symptom scales, a global health and quality-of-life scale and six single-item symptom measurements. This scale of items results in a score ranging from 0 to 100, where a higher score for the functional, global health and quality of life of respondents indicates better health.

In the symptom scales, a higher score indicates a greater number of symptoms (Aaronson, Ahmedzai et al. 1993). Single-symptom items are scored in the following manner: 0 refers to no symptoms, ≤33.33 indicates mild symptoms, ≤66.66 indicates moderate symptoms and ≤100 indicates severe symptoms. Multi-item symptoms are scored in the following manner: 0 indicates no symptoms, 0.01 to 66.65 indicates mild symptoms, 66.66 to 99.99 indicates moderate symptoms and 100 indicates severe symptoms.

4.6.3 Sociodemographic and clinical questionnaire

We also collected information on participants’ age and sex, weight, height, comorbidities, medication, smoking history and habits, family circumstances and occupational status.

4.7 Statistical analyses

4.7.1 Study I

In study I, statistical analyses were performed using NCSS 8 software (NCSS, LLC, Kaysville, UT, USA). We calculated survival using the Kaplan–Meier method.

4.7.2 Study II

In study II, using the Kaplan–Meier method, we calculated the outcome measurements of recurrence-free and overall survival.

4.7.3 Study III

In study III, our outcome measurements consisted of recurrence-free and overall survival, which we calculated using the Kaplan–Meier method. Differences were determined using the log-rank analysis, whilst the independent prognostic factors for survival and disease-free survival were analysed using the Cox proportional hazards regression analysis. All statistical analyses were performed using the NCSS 8 statistical software program (NCSS, East Kaysville, UT, USA). We considered $p \leq 0.05$ statistically significant.

4.7.4 Study IV

We present the study population characteristics as means with standard deviations (SDs), as medians with interquartile ranges (IQRs) or as numbers with percentages. Statistical comparisons between groups were calculated using the Fisher-Freeman-Halton test, student's t-test, permutation test or bootstrap-type analysis of variance (ANOVA) when appropriate. Adjusted comparisons between groups were evaluated using the bootstrap-type analysis of covariance (ANCOVA). Models included sex, age and CCI as covariates. The bootstrap method was used when the theoretical distribution of the test statistics was unknown or when assumptions were violated (e.g., non-normality). The adjusted correlation (partial) coefficients were calculated using the Pearson's r. For all analyses, we used Stata 15.1 (StataCorp LP, College Station, TX, USA).

5 RESULTS

5.1 Patients demographic characteristics (studies I–IV)

Table 9. Patient demographic characteristics (**studies I–IV**).

		Study I (n = 135)	Study II (n = 21)	Study III (n = 49)	Study IV (n = 55)
Age, in years	Median (Range)	60 (17–90)	59 (23–81)	57 (17–90)	68 (17–84)
Sex	Male Female	41 (30%) 94 (70%)	13 (62%) 9 (38%)	19 (39%) 30 (61%)	17 (31%) 38 (69%)
BMI, kg/m^2	Median (range)	25 (17–39)	26 (17–37)	26 (19–39)	26 (19–39)
Charlsson comorbidity index	Median (range)	2 (2–8)	3 (2–8)	2 (1–7)	2 (2–8)
Current smoking status	Yes No	19 116	3 18	8 41	10 45
History of oncological treatment	None Previous radiotherapy at site Previous chemotherapy Previous radiochemotherapy	62 50 22 1	16 5 0 0	28 16 5 0	32 16 7 0

BMI, Body mass index.

5.2 Indications for surgery (studies I–IV) and histological subtypes of soft-tissue sarcoma (study III)

In **study I**, a total of 135 patients underwent chest wall resection, amongst whom 118 also underwent chest wall reconstruction. The primary indications for resections consisted of breast cancer, soft-tissue sarcoma and bone sarcoma.

Study II describes our surgical technique for diaphragm and thoracoabdominal wall reconstruction following tumour resection, during which the most common indication for surgery was sarcoma. **Table 10** lists the indications for resections (**studies I–IV**).

Table 10. Indications for resection (**studies I–IV**).

		Study I (n = 135)	Study II (n = 21)	Study III (n = 49)	Study IV (n = 55)
Breast cancer	**Total**	**44**	**0**	**0**	**15**
	Primary (locally advanced)	7	0	0	2
	Recurrent / metastatic	37	0	0	13
Soft-tissue sarcoma	**Total**	**38**	**5**	**38**	**16**
	Primary	34	4	35	16
	Recurrent	3	1	1	0
	Metastatic	1	0	2	0
Osteo- or chondrosarcoma	**Total**	**28**	**9**	**0**	**14**
	Primary	26	8	0	13
	Recurrent	2	1	0	1
Desmoid tumour	**Total**	**11**	**2**	**11**	**5**
Metastases	**Total**	**7**	**4**	**0**	**3**
	Melanoma	2	1	0	0
	Colorectal cancer	2	1	0	2
	Epidermoid cancer	1	1	0	0
	Renal cancer	1	0	0	1
	Ovarian cancer	1	1	0	0
Other primary tumours	**Total**	**7**	**1**	**0**	**2**
	Solitary fibrous tumour	2	1	0	0
	Basosquamus carcinoma	1	0	0	1
	Neuroendocrine tumour	1	0	0	0
	Basal cell carcinoma	1	0	0	1
	Granular cell tumour	1	0	0	0
	Osteochondroma	1	0	0	0

Study III evaluated outcomes following chest wall resection amongst 49 soft-tissue sarcoma patients. Amongst these sarcomas, the most common subtype consisted of malignant fibrous histiocytoma (n = 15), with the histological sarcoma subtypes appearing in **Table 11**. Of these sarcomas, 31 (63%) were high grade and 18 (37%) were low grade.

Table 11. Soft-tissue sarcoma of the chest wall and their histological subtypes and grades (**study III**) (Kuwahara, Salo et al. 2019).

Histology	Grade 1	Grade 2	Grade 3	Grade 4	Total no. of patients
Malignant fibrous histiosytoma			4	11	15 (30.6%)
Desmoid tumour					11 (22.5%)
Fibrosarcoma		3		1	4 (8.2%)
Angiosarcoma			1	3	4 (8.2%)
Synovial sarcoma				3	3 (6.1%)
Liposarcoma	1		1		2 (4.1%)
Leiomyosarcoma			1	1	2 (4.1%)
Pleomorphic sarcoma				1	1 (2.0%)
Malignant peripheral nerve sheath tumour		1			1 (2.0%)
Malignant phylloid tumour			1		1 (2.0%)
Unclassified sarcoma		2	1	2	5 (10.2%)
Total	1	6	9	22	49 (100.0%)

Grading of soft-tissue sarcoma based on the Scandinavian four-grade system (Markhede, Angervall et al. 1982, Meis-Kindblom, Bjerkehage et al. 1999).

5.3 Chest wall resections (studies I–IV)

Study I included 72 full-thickness and 63 partial-thickness chest wall resections. Among the partial-thickness resections, 34 involved soft-tissue resections only and 29 involved skeletal bone resections. The most common anatomical site of a chest wall resection was anterolateral (n = 77, 57%). The median defect size for partial-thickness resections was 85 cm^2 (34.4–1400.0), climbing to 180 cm^2 (9.9–336.0) for full-thickness resections. **In study II**, a thoracoabdominal wall resection was combined with a diaphragm resection (**Figure 12,** page 34). **Table 12** summarises the operative resection characteristics (**studies I–IV**).

In **study I**, clear histological margins could be reached in 82% (n = 111) of the resections. In **study III** consisting of sarcoma patients only, resection margins were wide or marginal in 86% (n = 42) of cases.

In study I, the median operation time was 225 min (range 41–500 min). For microvascular free flaps, this time increased to 375 min (range 250–495 min). Typically, patients were extubated within 24 hours postoperatively. Extubation in the operating theatre was performed in 71 (53%) of cases and extubation took place in the intensive care unit (ICU) in 64 (47%) of cases. The median length of stay in ICU was 1 day (range 0–38). Full-thickness chest wall resection, an increased blood loss and prolonged operating time all associated with a significantly increased length of ICU stay ($p < 0.05$). Yet, patient age did not significantly correlate with length of ICU stay ($p = 0.077$).

Table 12. Operative characteristics (**studies I–IV**).

		Study I (n = 135)	Study II (n = 21)	Study III (n = 49)	Study IV (n = 55)
Location of resection	Anterolateral	77	0	25	30
	Thoracoabdominal	22	21	9	10
	Anterior (sternal)	21	0	6	9
	Posterolateral	12	0	7	4
	Extended forequarter amputation	4	0	2	2
Resection	Full-thickness resection	72	9	19	29
	Partial-thickness resection	63	12	30	26
	Defect size, cm^2, median (range)	156	178	157	177
Operative margin	Wide	29	4	14	15
	Marginal	82	12	28	36
	Intralesional	24	5	7	4

Wide, histological margin (>2.5 cm or intact fascia/pleura)
Marginal, histological margin (1 mm–2.5 cm)

5.4 Chest wall reconstructions (studies I–IV)

In **study I**, reconstruction of the chest wall was warranted in 118 (87%) of cases. Chest wall stabilisation was performed in 93 patients, whilst soft-tissue coverage alone with a flap proved sufficient for 25 patients. Chest wall stabilisation relied on mesh in 59 cases, 20 cases relied on the sandwich technique (methylmethacrylate between two meshes), 13 cases used free avascular rib grafts and a mesh and 1 case relied on Stratos® titanium bars (Medxpert, Max-Immelmann-Allee 19 79427 Eschbach, Germany).

Chest wall stabilisation with a concurrent soft-tissue flap was warranted in 57 (48%) cases. The remaining patients underwent either chest wall stabilisation or soft-tissue flap coverage. Overall, soft-tissue reconstruction with a flap was performed on 82 patients. Flap coverage was achieved with pedicled or local flaps in most cases (79%). The most common pedicled flap used was the ipsilateral musculocutaneus latissimus dorsi flap (n = 58, 70%). Free flaps were necessary in 21% of cases and the most common free flap was the TFL flap (n = 11, 14%). **Table 13** summarises the chest wall reconstruction procedures (**studies I–V**).

Table 13. Chest wall reconstructive procedures (**studies I–IV**).

	Study I (n = 135)	Study II (n = 21)	Study III (n = 49)	Study IV (n = 55)
Reconstruction type	**118** (87%)	**21** (100%)	**37** (76%)	**47** (85%)
Chest wall stabilisation + flap	**57**	**6**	**13**	**24**
Mesh + pedicular/local flap	20	2	5	10
Mesh and cement sandwich + pedicular/local flap	12	1	1	5
Mesh + rib graft + pedicular/local flap	11	0	1	3
Mesh + free flap	7	3	3	3
Mesh and cement sandwich + free flap	4	0	2	2
Mesh + rib graft + free flap	2	0	0	1
Mesh + Stratos† + pedicular/local flap	1	0	1	0
Chest wall stabilisation only	**36**	**14**	**13**	**15**
Mesh	32	14	13	13
Mesh and cement sandwich	4	0	0	2
Soft-tissue flap coverage only	**25**	**1**	**11**	**8**
Pedicular/local flap	21	1	10	7
Free flap	4	0	1	1
Primary chest wall closure	**17** (13%)	**0** (0%)	**12** (24%)	**8** (15%)
All	**135** (100%)	**21** (100%)	**49** (100%)	**55** (100%)

†Strasbourg Thoracic Osteosyntheses System (MedXpert GmbH, Eschbach, Germany).

In **Study II**, 15 cases involved reattaching the resected diaphragm with an acceptable tension to the thoracoabdominal wall. Diaphragm reconstruction with mesh was warranted in six cases. Thoracoabdominal wall stabilisation with mesh was performed in 14 cases. Six patients underwent thoracoabdominal wall reconstruction with mesh and a soft-tissue flap (free flap, n = 3; pedicled flap, n = 3). In one case, a flap reconstruction alone was sufficient for thoracoabdominal wall reconstruction. **Table 14** shows the surgical treatments in **study II**.

Table 14. Surgical treatment in **study II**.

Patient No.	Diaphragm resection, cm	Diaphragm reconstruction (type of mesh)	Thoracoabdominal wall reconstruction
1	1	Resutured	Mesh and free TFL
2	2	Resutured	Mesh
3	5	Mesh (Gore-Tex)	Mesh
4	3	Resutured	Mesh
5	6–7	Resutured	Mesh
6	3	Resutured	Mesh
7	2	Resutured	Mesh and pedicled LD
8	4	Mesh (Parietex)	Mesh
9	2	Resutured	Mesh
10	2	Resutured	Mesh
11	3	Resutured	Mesh
12	5	Mesh (Proceed)	Mesh
13	2	Resutured	Mesh and free TFL
14	2	Resutured	Mesh and Free TFL
15	4	Mesh (Prolene)	MMS and pedicle LD
16	3	Resutured	Mesh
17	1	Resutured	Pedicled LD
18	2	Resutured	Mesh
19	2	Resutured	Mesh and pedicled LD
20	6	Mesh (Parietex)	Mesh
21	3	Resutured	Mesh

TFL, tensor fascia lata; LD, latissimus dorsi; MMS, methylmethacrylate ‘sandwich’ technique.

5.5 Complications (studies I–IV)

Across all studies (**studies I–IV**), we observed no 30-day mortality and no flaps were lost. In **study I**, however, 90-day mortality was 4.4%. **Table 15** summarises the CD classification of complications (**studies I–IV**), although grade I complications were not evaluated.

Amongst 135 patients, 29 (21%) faced complications in **study I**. The most common complications involved partial flap loss (n = 8, 5%), pneumonia (n = 7, 5%) and cardiac-related complications (n = 6, 4%). In total, 19 re-operations were needed. In our statistical analyses, preoperative RT did not statistically significantly increase the incidence of wound complications (p = 0.595). A more complex reconstruction (chest wall stabilisation and flap), intralesional surgical margins, increased blood loss and operation time all associated with a significantly increased risk of complications ($p < 0.05$). The rate of major complications (CD grade IIIa or higher) in **studies I through IV** were 12.6%, 4.8%, 10.2% and 7.3%, respectively.

In **study II**, we observed no abdominal wall hernias or paradoxical chest wall movement following thoracoabdominal wall and diaphragm reconstructions. In **study III**, 11 patients experienced a complication, most commonly involving a wound infection (n = 4) following artery/vein thrombosis of the flap.

Table 15. Clavien–Dindo classification of surgical complications (**studies I–IV**).

	Study I	Study II	Study III	Study IV
Total no. of patients	**135**	**21**	**49**	**55**
Total no. of complications	**29** (21%)	**5** (24%)	**11** (22%)	**9** (16%)
Grade				
Grade II	12	4	6	5
Grade IIIa	4	1	1	2
Grade IIIb	10	0	4	0
Grade Iva	3	0	0	2
Grade IVb	0	0	0	0
Grade V	0	0	0	0

5.6 Oncological outcomes (studies I–IV)

In **study I**, the average follow-up time reached 68 (range 2–232) months, with a median of 49 months. We calculated survival for all patients **(Figure 23)** using the Kaplan–Meier method, categorising patients based on subgroups of chondro- or osteosarcoma, soft-tissue sarcoma and advanced breast cancer. **Table 16** shows the 1-, 2- and 5-year overall survival rates.

In **study II**, the median follow-up time was 39 months, for which 1- and 5-year overall survival rates were 85.7% and 65.9%, respectively.

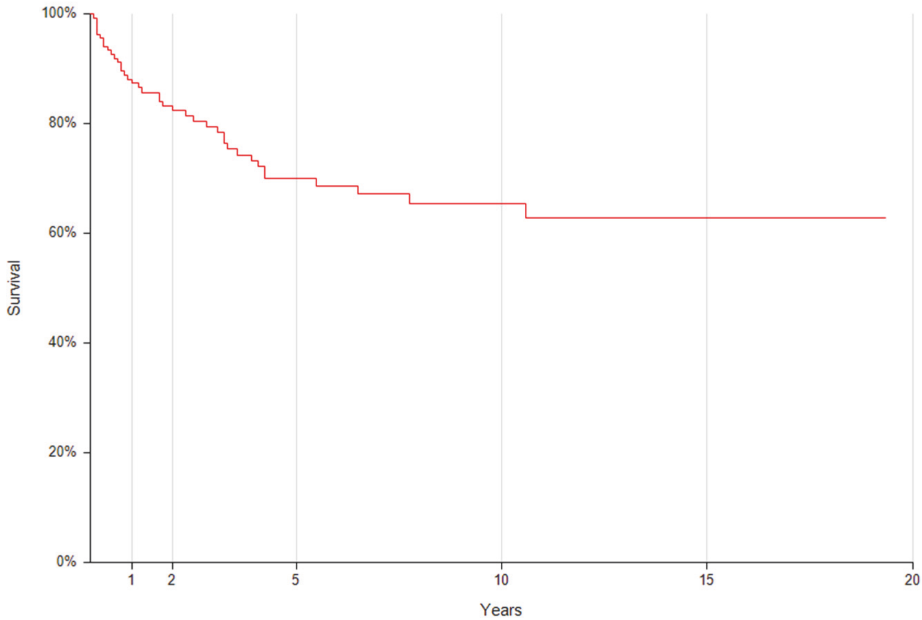

Figure 23. Survival for all patients (**study I**). (Reproduced with permission from *Plastic and Reconstructive Surgery* (Salo, Tukiainen 2018).)

Table 16. Survival following chest wall resection and reconstruction (**study I**).
(Reproduced with permission from *Plastic and Reconstructive Surgery* (Salo, Tukiainen 2018).)

	All (n = 135)	Bone or chondrosarcoma (n = 28)	Soft-tissue sarcoma (n = 38)	Advanced breast cancer (n = 44)
30-day mortality, %	0%	0%	0%	0%
90-day mortality, %	4.4%	3.6%	2.6%	9%
1-year survival, %	84%	96%	92%	73%
2-year survival, %	82%	88%	85%	68%
5-year survival, %	70%	88%	71%	53%

In **study III**, the median follow-up time exceeded 7 years. Oncological adjuvant treatment was administered to 18 patients (11 radiotherapy, 6 chemotherapy and 1 both modalities). In addition, 1-, 5- and 10-year overall survival amongst chest wall soft-tissue sarcoma patients reached 94%, 76% and 72% **(Figure 24)** with recurrence-free rates falling to 84%, 71% and 71%. In our statistical analyses, treatment (radical or nonradical; p = 0.04), margins (wide, marginal or intralesional; p = 0.02) and age (p = 0.02) significantly impacted overall survival in patients (**Table 17)**. Furthermore, none of the variables significantly impacted disease-free survival.

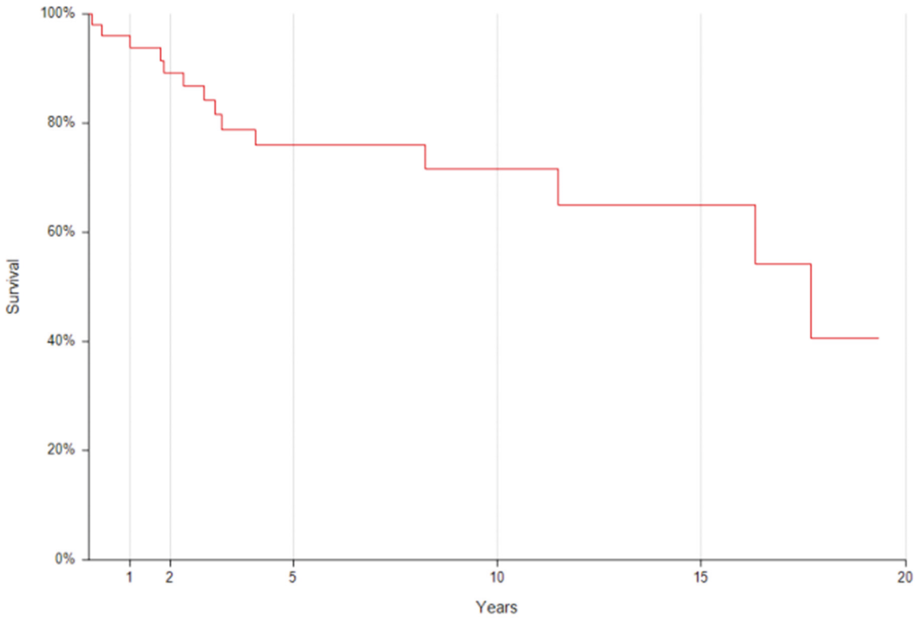

Figure 24. Overall survival amongst chest wall sarcoma patients (**study III**). (Reproduced with permission from the *Annals of Plastic Surgery* (Kuwahara, Salo et al. 2019).)

Table 17. Overall survival and disease-free survival (n = 38), excluding desmoid tumour patients (study III). (Reproduced with permission from the Annals of Plastic Surgery (Kuwahara, Salo et al. 2019).)

Variable and categories	n	5-year OSR, %	p	5-year DFSR, %	p
Treatment					
Radical	20	80.3	0.04*	80.7	0.29
Nonradical	18	47.5		64.3	
Margin					
Wide margin	14	85.1	0.02*	84.6	0.05
Marginal margin	21	61.9		70.2	
Intralesional margin	3	0		0	
Grade					
Low grade	7	100	0.05	100	0.09
High grade	31	60.8		67.1	
Adjuvant therapy					
Resection + adjuvant	16	52.5	0.36	58.6	0.10
Resection only	22	79.5		85.0	

Radical treatment: resection with a wide margin (>2.5 cm or intact fascia/pleura) or marginal margin resection (1 mm–2.5 cm) with radiotherapy.
Resection + adjuvant: patients underwent tumour resection and adjuvant radiotherapy or/and chemotherapy.
*p < 0.05.
OSR, overall survival rate; DFSR, disease-free survival rate.

5.7 Health-related quality of life following oncological resection and reconstruction of the chest wall (study IV)

In total, 55 patients (response rate 71%) with a mean (±SD) age of 68 (±14) years completed the HRQoL questionnaires a median 66 (IQR 38–141) months following surgery.

We compared respondents (n = 55) and nonrespondents (n = 23), finding that nonrespondents were significantly younger than respondents (7 years younger).

In a comparison of HRQoL (15D) of patients to the control population, the mean patient 15D score (0.878, SD ±0.111) was comparable to the control population (age- and gender-standardised) (0.891, SD ±0.041) without statistically significant difference. The patient group significantly differed along two dimensions: patients reported lower scores for 'usual activities' (p = 0.043) and 'breathing' (p = 0.027; **Figure 25**).

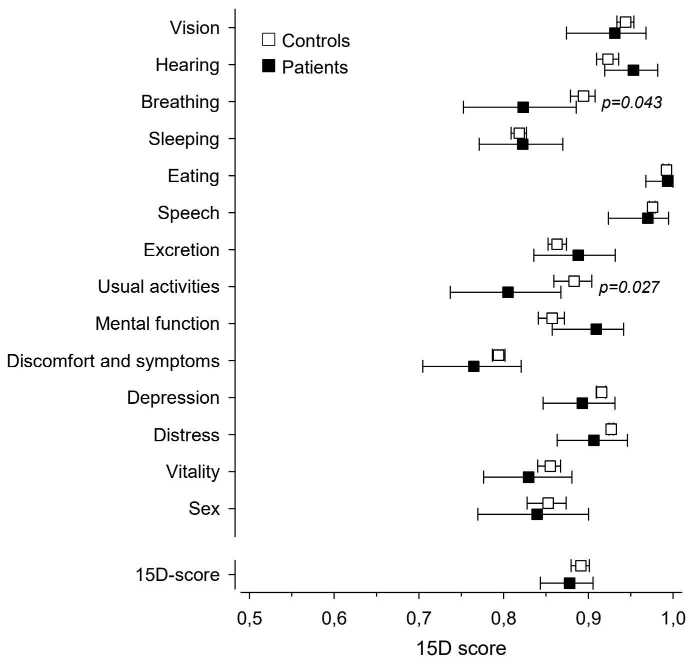

Figure 25. The mean 15D dimension scores and the total 15D score for patients who underwent chest wall reconstruction (n = 55) compared to scores for the age- and gender-standardised general population (**study IV**). (Reproduced with permission from the *Journal of Plastic, Reconstructive & Aesthetic Surgery* (Salo, Repo et al. 2019).)

In a comparison of different reconstruction types based on demographic and surgical characteristics, we observed a statistically significant difference in diagnosis, full-thickness resection and CCI (**Table 18**).

Table 18. Patient demographic and perioperative characteristics for different reconstruction types (study IV). (Reproduced with permission from the *Journal of Plastic, Reconstructive & Aesthetic Surgery* (Salo, Repo et al. 2019).)

	Reconstruction type				p
	Primary closure n = 8	Chest wall stabilisation n = 15	Soft-tissue flap n = 8	Chest wall stabilisation + flap n = 24	
Mean age, in years, (SD)	72 (8)	62 (17)	75 (13)	67 (14)	0.15
Female, n (%)	7 (88)	10 (67)	5 (62)	16 (67)	0.75
BMI, mean (SD)	27.8 (3.3)	25.1 (3.2)	27.0 (5.9)	25.6 (3.6)	0.37
Charlsson comorbidity index, mean (SD)	2.1 (0.4)	3.1 (1.8)	3.9 (2.2)	3.8 (2.0)	<0.001
Diagnosis, n (%)					0.002
Advanced breast cancer	0 (0)	3 (20)	0 (0)	12 (50)	
Soft-tissue sarcoma	5 (62)	3 (20)	5 (62)	3 (13)	
Chondro- or bone sarcoma	2 (25)	5 (33)	0 (0)	7 (29)	
Others	1 (13)	4 (27)	3 (38)	2 (8)	
Chest wall full-thickness resection, n (%)	0 (0)	3 (20)	2 (25)	24 (100)	<0.001
Mean defect size, cm^2, (SD)	162 (63)	130 (127)	209 (116)	201 (128)	0.26
Adjuvant therapy, n (%)	3 (38)	5 (33)	2 (25)	13 (54)	0.44
Recurrence during follow-up, n (%)	0 (0)	2 (13)	0 (0)	2 (8)	0.71
Metastasis during follow-up, n (%)	0 (0)	1 (7)	0 (0)	3 (13)	0.81
Median time after primary surgery, in months, median (range)	92 (16–241)	59 (18–229)	59 (33–207)	73 (29–240)	0.44

When comparing quality of life (15D and QLQ-C30) amongst the different reconstruction types, we found no statistically significant difference following adjustments (i.e., for sex, age and CCI; **Table 19**).

Table 19. Mean 15D scores and mean EORTC QLQ-C30 scores for patients who underwent chest wall reconstruction based on reconstruction type (study IV). (Reproduced with permission from the *Journal of Plastic, Reconstructive & Aesthetic Surgery* (Salo, Repo et al. 2019).)

	Reconstruction type				p	
	Primary closure n = 8 Mean (SD)	Chest wall stabilisation n = 15 Mean (SD)	Soft-tissue flap n = 8 Mean (SD)	Chest wall stabilisation + flap n = 24 Mean (SD)	Crude	Adjusted*
EORTC QLQ-C30:						
Global health status/ QoL	79 (17)	69 (22)	64 (27)	76 (17)	0.38	0.53
Functional scales						
Physical	79 (27)	74 (31)	63 (31)	86 (14)	0.14	0.17
Role	83 (24)	79 (29)	65 (46)	90 (15)	0.24	0.35
Emotional	94 (10)	84 (18)	74 (25)	91 (11)	0.095	0.29
Cognitive	92 (18)	86 (22)	81 (24)	94 (10)	0.25	0.58
Social	98 (6)	90 (16)	75 (33)	95 (13)	0.11	0.55
15D:						
Total score	0.881 (0.069)	0.862 (0.116)	0.798 (0.199)	0.910 (0.060)	0.18	0.28
Mobility	0.907 (0.264)	0.943 (0.119)	0.871 (0.269)	0.921 (0.179)	0.89	0.93
Vision	1.000 (0.000)	0.957 (0.089)	0.792 (0.211)	1.000 (0.000)	0.003	0.51
Hearing	0.937 (0.116)	0.810 (0.301)	0.778 (0.346)	0.832 (0.221)	0.20	0.25
Breathing	0.701 (0.307)	0.769 (0.185)	0.766 (0.285)	0.836 (0.154)	0.44	0.45
Sleeping	1.000 (0.000)	0.984 (0.062)	1.000 (0.000)	1.000 (0.000)	0.23	0.26
Eating	1.000 (0.000)	0.923 (0.220)	0.912 (0.164)	1.000 (0.000)	0.12	0.16
Speech	0.815 (0.154)	0.960 (0.104)	0.724 (0.278)	0.938 (0.123)	0.014	0.34
Excretion	0.921 (0.146)	0.777 (0.307)	0.770 (0.269)	0.897 (0.195)	0.28	0.19
Usual activities	0.822 (0.215)	0.792 (0.315)	0.686(0.308)	0.848 (0.167)	0.52	0.46
Mental functioning	0.911 (0.165)	0.929 (0.148)	0.822 (0.191)	0.926 (0.148)	0.53	0.64
Discomfort	0.776 (0.213)	0.761 (0.168)	0.689 (0.365)	0.788 (0.187)	0.88	0.17
Depression	0.883 (0.126)	0.858 (0.151)	0.794 (0.264)	0.951 (0.097)	0.053	0.43
Distress	0.931 (0.127)	0.874 (0.171)	0.767 (0.219)	0.966 (0.093)	0.024	0.84
Vitality	0.854 (0.178)	0.796 (0.179)	0.735 (0.320)	0.874 (0.156)	0.40	0.45
Sexual activity	0.819 (0.307)	0.758 (0.346)	0.858 (0.213)	0.891 (0.144)	0.49	0.40

*Adjusted for sex, age and Charlson comorbidity index.

6 DISCUSSION

6.1 General considerations

Oncological resection and reconstruction of the chest wall present a surgical challenge due to the complex anatomy of the chest wall, the need to preserve the protective function for vital organs and the functional importance in respiratory physiology. This thesis demonstrates that chest wall resection and reconstruction can be performed safely. Achieving this demands careful patient selection, appropriate peri- and postoperative treatment, meticulous planning and selection of the surgical technique and a multidisciplinary team approach.

Resection with wide margins should also remain the aim of treatment for sarcomas located in the chest wall and when the patient is treated with a curative intent. If wide margins cannot be achieved, adjuvant radiotherapy should be administered when possible. However, this may not always be feasible given a previous history of RT. This infeasbility applies to cases of recurrent sarcoma when radiotherapy is administred primarily as well as for post-radiation sarcomas.

This study also demonstrates that surgical resection and appropriate reconstruction currently plays an important role in treating patients with locally advanced breast cancer. Survival amongst advanced breast cancer patients has also improved given the evolution of oncological therapies. This notwithstanding, in many cases, patients appear to benefit from surgery and, therefore, a surgical approach should at least be considered.

After chest wall reconstruction following tumour resection, patient HRQoL remains comparable to that of the age- and gender-standardised general population.

6.2 Resection and reconstruction outcomes

6.2.1 Chest wall

Major chest wall operations pose potentially high risks to patients and, thus, a careful and multidisciplinary patient evaluation is essential to achieving the best possible results. All sarcoma patients were reviewed during a sarcoma multidisciplinary team (MDT) meeting, whilst patients with advanced breast cancer were evaluated during a breast cancer MDT meeting or, in some cases, treated in co-operation with an oncologist. With careful MDT planning, the optimal timing of surgical and possible oncological treatment can be achieved.

En-bloc tumour resection remains the priority for chest wall malignant tumour resection. This principle should not be compromised because of a resultant defect. In study I, the median resection defect size was 156 cm^2, reflecting the tumour size and our aim of achieving wide surgical margins. Our defect size and the amount of full- and partial-thickness resections agree with other reports in the literature, thus permitting us to compare our reconstruction methods to other published series (Daigeler, Druecke et al. 2009, Chang, Mehrara et al. 2004, Giordano, Garvey et al. 2020, Deschamps, Tirnaksiz et al. 1999).

Our definition of the surgical margins for both sarcoma and breast cancer patients in studies I through IV relied on Enneking's classification (Enneking, Spanier et al. 1980). In our studies, we paid particular attention to the surgical margins because in aggressive sarcomas or breast tumours every effort should be made to avoid cutting into the tumour resulting in an intralesional excision and potential tumour dissemination. In addition, the surgical margins are not well defined in many other studies. We plan our chest wall resections with large surgical margins given that in the final histological examination the malignant tumour margins may extend beyond those anticipated based on radiological findings. If the thoracic cavity has been opened and the surgical margins are intralesional, the entire thoracic cavity can be contaminated. Intra-operative frozen section was only used in exceptional cases since it is difficult to evaluate malignancy in sarcomas and establishing a frozen section of the bone is impossible.

In study I, we achieved clear surgical margins in 82% of cases, the primary goal in curative oncological surgery. In 18% of cases, the margins were intralesional, an acceptable rate when considering that some surgeries were performed with a palliative intent. Other major chest wall resection and reconstruction series did not report their surgical margins in oncological cases (Mansour, Thourani et al. 2002, Chang, Mehrara et al. 2004, Daigeler, Druecke et al. 2009).

Furthermore, the classification of surgical margins in sarcoma surgery is not uniform with varying interpretations of margins from different studies. Therefore, comparing studies remains challenging. In study III, which consisted of soft-tissue sarcoma patients, wide (28.6%) or marginal (57.1%) surgical margins were achieved in the vast majority (85.7%) of cases. Intralesional surgical resection margins in the remaining 7 (14.3%) patients included 4 desmoid tumour patients. The infiltrative growth pattern of desmoid tumours may help explain this finding. In other sarcoma series, clear margins were achieved in 85.1% (Shewale, Mitchell et al. 2018), 97.7% (Tsukushi, Nishida et al. 2009) and 100% of cases (Gross, Younes et al. 2005). Soerensen et al. (2019) did not differentiate between marginal and intralesional resections in their study, with the resection margin reported as marginal or intralesional in 34% of cases.

In our series, we used mesh to prevent any bulging or herniation of the lung if a defect included the resection of two ribs. Mansour et al. also reported a similar use of mesh (Mansour, Thourani et al. 2002). In previous studies, chest wall stabilisation is recommended in defects over 5 cm, roughly equivalent to the width of two ribs (Harati, Kolbenschlag et al. 2015, Netscher, Baumholtz 2009).

Our choice of mesh used in stabilisation relies on the surgeon's preference and experience, with the price of mesh also representing an important factor. This approach agrees with that used in other centres, given that currently none of the mesh types have demonstrably performed better than others (Khullar, Fernandez 2017, Mahabir, Butler 2011).

For larger anterolateral or anterior chest wall defects (resection involving three or more ribs) requiring additional stabilisation, we used the more rigid sandwich technique or (in earlier cases) a rib graft with mesh. The sandwich technique was also used in extended forequarter amputation cases. Several other researchers have also recommended the use of a more rigid stabilisation technique in large anterolateral or anterior chest wall defects (Lardinois, Muller et al. 2000, Harati, Kolbenschlag et al. 2015). In thoracoabdominal resections, which may include the resection of caudal ribs (VII–XII) or in posterolateral resections, additional stabilisation was not typically used in our patients. Losken et al. and Deschamps et al. adopted a similar philosophy regarding posterior chest wall stabilisation owing to scapula support (Losken, Thourani et al. 2004, Deschamps, Tirnaksiz et al. 1999).

Our experience with the sandwich technique has been favourable, whereby we have observed multiple benefits from this method. These include a short operating time, its cost-effectiveness and the individually designed size and shape of the prosthesis. Other authors have reported similar experiences using the sandwich technique (Lardinois, Muller et al. 2000, Chang, Mehrara et al. 2004). However, Weyant et al. (Weyant, Bains et al. 2006) reported a higher incidence of wound infection using the sandwich technique in comparison with other prostheses. In our studies, the sandwich technique did not impact wound infection rates.

The use of bioprosthetic materials in chest wall stabilisation has become more popular in recent years. At the time of this study, we have not used these materials in adult patients requiring chest wall reconstruction given the lack of long-term results with this expensive material. However, we have used bioprosthetic materials in growing children, although these experiences have not been included in this thesis. Recently, Giordano et al. reported fewer surgical site complications when using an ADM compared to a synthetic mesh (Giordano, Garvey et al. 2020). Results from the use of bioprosthetic material in contaminated abdominal wall repairs appear encouraging (Rosen, Krpata et al. 2013, Alaedeen, Lipman et al. 2007). Such results support the use of bioprosthetic materials in cases that carry a high risk of infection.

Likewise, our experience in the use of titanium bars remains limited. We have used them in only one reconstruction, whereby a late complication necessitated the removal of broken bars. Berthed et al. also reported an extremely high complication rate of 44% in a long-term follow-up study of titanium bars (Berthet, Gomez Caro et al. 2015).

The erosion of the major mediastinal vessels and the heart represent potential risks when foreign material such as coarse meshes alone or with an MMA plate is used. Postoperatively during long-term follow-up, the shape and form of the thorax can slowly change following resection and reconstruction. This can lead to a loosening or dislocation of the prosthetic material, which can turn over or fold inside the thorax, leading to the compression or even erosion of cardiovascular structures. To minimise this risk, a mesh is always sutured via drill holes to the outer surface of the bony or cartilaginous thorax under tension, which is maintained with firm nonabsorbing sutures. In addition, a thin MMA plate smaller than the actual bony defect is carefully molded to resemble the original curved form of the chest wall. Following the resection of the manubrium and the first and second ribs, special attention must be paid to prevent any compression of the great vessels and trachea at the cranial aspect through the use of an anatomically curved MMA plate.

In soft-tissue reconstruction, we adhered to the reconstructive 'elevator' rather than 'ladder' technique (Gottlieb, Krieger 1994). Our use of skin grafts in chest wall soft-tissue reconstruction remained rather limited given that these techniques were suboptimal for this type of reconstruction, requiring coverage of exposed bone, cartilage or prosthetic materials.

Soft-tissue reconstruction with flaps provides good, well-vascularised coverage of the chest wall bony cage, prosthesis or mesh. Pedicled myocutaneous flaps with a constant anatomy served as our first choice for soft-tissue reconstruction of the chest wall when these flaps were available and the size and dimension of the flap was adequate. Our flap selection agrees with other studies (Losken, Thourani et al. 2004, Daigeler, Druecke et al. 2009, Chang, Mehrara et al. 2004).

Similar to many other previous studies (Losken, Thourani et al. 2004, Daigeler, Druecke et al. 2009), the latissimus dorsi flap is considered the workhorse for reconstruction of chest wall defects. The primary reasons to consider the latissimus dorsi flap as the first option consist in its constant anatomy, the large skin island and the reliability of the flap.

Some authors have preferred the pedicled rectus abdominis (Weyant, Bains et al. 2006) or pectoralis major flap (Arnold, Pairolero 1996). We also used the pectoralis major flap in reconstruction following sternal infection. The low usage rate of the pectoralis flap in our series stems from the fact that these sternal infection cases were not included in this thesis unlike the study by Arnold et al. (Arnold, Pairolero 1996).

We used the rectus abdominis flap in only one case given the potential detrimental impact on breathing during the postoperative period and the risk of an abdominal wall hernia. Our flap selection also reflects our aim to avoid any increase in the chest wall defect size when closing the flap donor site. In addition, we based our choice of flap on its location lieing beyond any possible previous RT area.

In three cases, we used the mammary gland by mobilising it as a local flap. This can represent a valuable and straightforward option in special circumstances such as in a highly morbid elderly patient.

When pedicled or local flaps were unavailable or inadequate in dimension or size, we performed a microvascular free-flap reconstruction. For a microvascular reconstruction, careful planning is important in order to ensure a safe and efficient operation.

In free-flap reconstruction, our first choice consisted of flaps from the thigh area. Using the thigh as the donor site carries several advantages. These advantages include offering many variations for the flap composition (TFL, ALT, rectus femoris and vastus lateralis), a large potential flap (30 x 40 cm) and the flap can normally be harvested with the patient in the same position (supine or lateral) as during resection. Furthermore, a two-team approach is possible, thereby minimising the operation time. In addition, the thigh donor site does not compromise respiratory functioning in contrast to flaps harvested from the abdomen or chest area.

In study I, a microvascular free flap was necessary in 21% of cases, a rate somewhat higher than previous studies (Mansour, Thourani et al. 2002, Losken, Thourani et al. 2004, Chang, Mehrara et al. 2004).

In clinical work, the results of this thesis confirmed our surgical treatment protocol in chest wall resections and reconstructions in sarcoma and advanced breast cancer patients. This thesis highlights work and cooperation decided upon during MDT meetings as well as with planned intensivists.

6.2.2 Diaphragm

A combined resection of part of the diaphragm and thoracoabdominal wall represents a rather rare operation, indicated when a tumour is located close to the distal diaphragm either in the abdomen or the chest wall, such as that we employed in study II (Mansour, Thourani et al. 2002). In the reconstruction of combined thoracoabdominal wall and diaphragm defects, we applied similar principles to those employed for isolated chest wall reconstructions, although we did not rely on the sandwich technique. In our experience, an excessively rigid reconstruction is unnecessary in this region and may impair movement of the abdominal wall.

We used a mesh for diaphragm reconstruction if the defect exceeded 3 to 4 cm in order to avoid a flat drum-head diaphragm, which can lead to excess tension, limiting diaphragm movement and increasing the risk of hernia. Bax et al. emphasised in their report that reconstruction of a diaphragmatic dome is important to achieving a more functional diaphragm (Bax, Collins 1984). In addition, Finley et al. concluded that a defect up to 8 cm in size can be closed primarily (Finley, Abu-Rustum et al. 2009).

We used several different meshes in diaphragm reconstructions. Our choice of mesh relied on the surgeon's preference. According to the literature, the mainstay for reconstruction of the diaphragm has relied on the use of mesh (Finley, Abu-Rustum et al. 2009, Bassuner, Rice et al. 2017), although bioprosthetic materials have been used in the last decade (Asai, Watanabe et al. 2011, Bassuner, Rice et al. 2017). In view of our satisfactory results with synthetic meshes (a very low complication rate and no herniation), we have not employed bioprosthetic materials (Bassuner, Rice et al. 2017) or autologous reconstruction methods (Yamashita, Asai et al. 2020, Joshi, Sen et al. 2005).

6.3 Oncological outcomes

In order to meaningfully evaluate oncological survival, we applied a follow-up time of at least four years. The median follow-up times in studies I and III were 49 and 86 months, respectively. In study I, the 1-, 3- and 5-year survival rates for all patients, including all cancer types and metastatic cases, reached 84%, 82% and 70%, respectively.

Patients were divided into subgroups (study I) according to the histology of the tumours, with the highest survival found amongst chondro- and bone sarcoma patients, an expected result. The 1-, 3-, and 5-year survival rates were 96%, 88% and 88%, respectively. The 5-year survival rate from our study agrees with that from other studies: 64% (Burt, Fulton et al. 1992), 77% (Gao, Zhou et al. 2019) and 92% (Fong, Pairolero et al. 2004).

In advanced breast cancer patients, 5-year survival reached 53%. This result was encouraging, such that chest wall resection can represent a reasonable option. Advances in oncological treatment have also likely contributed to this improved survival. Traditionally, breast cancer patients with locally advanced disease have been regarded as poor surgical candidates given their anticipated poor prognosis based on older studies. However, wide variation exists in the 5-year survival rates reported: 69% (Petrella, Radice et al. 2016), 63% (Levy Faber, Fadel et al. 2013), 9% (Daigeler, Druecke et al. 2009) and 41% from meta-analyse (Wakeam, Acuna et al. 2017). Our findings agree with these studies, except for the low survival rate reported by Daigeler et al., which may reflect their high rate of palliative surgery (40%) (Daigeler, Druecke et al. 2009).

The survival rate amongst soft-tissue sarcoma patients in study III falls between that for chondro- and bone sarcoma patients and advanced breast cancer patietns. Our 5- and 10-year survival rates reached 76% and 72%. The highest 5-year survival rate of 88% was reported by Tsukushi et al. (Tsukushi, Nishida et al. 2009). The range of 5-year survival rate from other studies varied from 55% to 87% (Soerensen, Raedkjaer et al. 2019, Pfannschmidt, Geisbusch et al. 2006, Gross, Younes et al. 2005). However, these results must be compared cautiously owing to the varying numbers of high-grade tumours in these studies. For example, the study by Tsukushi et al. (Tsukushi, Nishida et al. 2009) comprised only 50% of patients with high-grade sarcomas, in contrast to the study by Soerensen et al. (87%) (Soerensen, Raedkjaer et al. 2019) or 63% in our study.

In statistical analyses, we found that being under 50 years old (p = 0.02), undergoing radical treatment (p = 0.04) and achieving a wide margin (p = 0.02) served as independent positive prognostic factors for chest wall sarcoma patients. Recently, Sorensen et al. also reported wide margins as a positive prognostic factor (Soerensen, Raedkjaer et al. 2019). In addition, Harati et al. and Tsukushi et al. also demonstrated that being less than 50 years represented a positive prognostic factor (Harati, Kolbenschlag et al. 2018, Tsukushi, Nishida et al. 2009). In our study, patients with a high-grade tumour have a 5-year overall survival rate of 60.8% and patients with a low-grade tumour exhibited an overall survival rate of 100%. Given our small sample size, we were unable to demonstrate a statistically significant difference in tumour grade as opposed to some other studies (Soerensen, Raedkjaer et al. 2019, Pfannschmidt, Geisbusch et al. 2006, Gross, Younes et al. 2005, Tsukushi, Nishida et al. 2009).

6.4 Complications

The CD classification (Dindo, Demartines et al. 2004) was developed to categorise surgical complications according to their severity, the type of therapy needed to correct the complication and to allow for more precise comparisons across different studies. This classification consists of seven different complication grades (I, II, IIIa, IIIb, Iva, IVb and V).

We used the CD classification of surgical complications in all four studies (studies I–IV) in this thesis. We did not estimate CD grade I complications since these are quite mild complications and their estimation is rather difficult, equivocal and possibly irrelevant in major surgery. Unfortunately, thus far, only one other study (Corkum, Garvey et al. 2020) relied on the CD classification in chest wall resections and reconstructions, thus rendering comparisons of complications between studies challenging.

In study I, our complication rate of 21.4% was lower than that reported in most other studies (**Table 6**, page 53). We identified a relatively low number of patients experiencing major complications (12.5%). Late complications remained rare, occurring in only two cases (a broken titanium barrier and an abdominal wall hernia following inadequate stabilisation of the thoracoabdominal wall without a mesh). Due to infection or any other reason, our prosthesis removal rate was zero. Weyent et al. reported a prosthesis removal rate of 3.8%, whilst Daigeler at al. reported a removal rate of 6.5% (Weyant, Bains et al. 2006, Daigeler, Druecke et al. 2009).

In study II, only 1 patient (5%) experienced major complications, although the total complication rate in study II reached 23.8%.

One possible reason for our relatively low rate of wound and infection complications could lie in our liberal use of flaps if the operation area was previously radiated. Furthermore, we may use microvascular flaps (free-flap rate 21%) more frequently than others. For example, in other large series, free-flap rates reached only 6% (Chang, Mehrara et al. 2004), 10% (Losken, Thourani et al. 2004) and 11% (Mansour, Thourani et al. 2002).

Weyant et al. reported that the sandwich technique reconstruction resulted in a higher wound complication rate than with other prostheses (Weyant, Bains et al. 2006). In study I, the stabilisation method appeared not to impact the complication rate. In our experience, the sandwich technique appears to work quite well. We used antibiotic cement and special care was taken to cover the stabilisation with well-vascularised soft tissue.

When justifying these rather long and extensive procedures, it is important to consider and report mortality as well as quality of life following surgery. In the present study, we found an operative (30-day) mortality rate of zero. This may reflect appropriate patient selection, surgical planning and technique and postoperative treatment, physiotherapy and aftercare. In other studies, the highest 30-day mortality rate following chest wall reconstruction was 7% (Mansour, Thorani et al. 2002), falling to as low as 2.3% (Lans, van der Pol et al. 2009).

In study I, 90-day mortality impacted 6 of 135 patients (4.4%). This mortality reflects the biological nature and extent of the underlying tumour. Most of these patients underwent surgery with a palliative intent, aiming to relieve tumour symptoms, such as ulceration, bleeding, infection, odour and pain, all of which diminish the quality of life of patients. Such symptoms may also prevent the use other forms of palliative therapies, including radiotherapy or chemotherapy. In other studies, the reported 90-day mortality was 6.2% (Giordano, Garvey et al. 2020) and 8.5% (Corkum, Garvey et al. 2020).

Based on our experience, surgery should be undertaken before the tumour extends too widely or metastasises. The decision to proceed with surgery should be based on recent radiological studies in order to gain realistic information about the extent of tumour involvement locally, regionally and systemically. In addition, certain tumour types (such as some myxoid or chondroid tumours) may rupture and disseminate locally in the chest cavity causing rapid tumour progression if resection is attempted too late relative to disease progression.

6.5 Health-related quality of life

In study IV, we found that the generic long-term HRQoL amongst patients undergoing chest wall reconstruction following oncological resection is comparable to the age- and gender-standardised general control population. However, along two dimensions ('breathing' and 'usual activities') from the 15D questionnaire, patients faired significantly poorer. Yet, in this study, we observed no statistically significant difference in the various types of reconstructions.

HRQoL and above all patient-reported outcome research have emerged as important components of cancer studies, currently forming one endpoint to research. Until recently, knowledge of long-term HRQoL after chest wall reconstruction following oncological chest wall resection remained limited. Only a small number of heterogenous HRQoL studies (n = 5) have investigated patient-reported outcomes following chest wall–related tumour studies (Heuker, Lengele et al. 2011, Daigeler, Druecke et al. 2009, Liu, Wampfler et al. 2017, Nakao, Miyata et al. 1986, Tacconi, Ambrogi et al. 2012). All previous studies feature some limitations, such as the following: a small sample size (Daigeler, Druecke et al. 2009, Heuker, Lengele et al. 2011, Nakao, Miyata et al. 1986, Tacconi, Ambrogi et al. 2012); no comparison of results to those amongst the general population (Heuker, Lengele et al. 2011, Nakao, Miyata et al. 1986, Tacconi, Ambrogi et al. 2012, Liu, Wampfler et al. 2017); no mention of the need for the reconstruction, the reconstruction method or the extent of the surgical procedure (Daigeler, Druecke et al. 2009, Liu, Wampfler et al. 2017); and missing information on patient diagnosis (Heuker, Lengele et al. 2011).

In contrast to these previous limitations, we compared our results to a sample from an age- and gender-standardised control population. Our sample size (n = 55) was favourable, consisting of accurate reporting of the patient diagnosis, the extent of the surgery and oncological treatment.

In our study, we observed that limitations along the breathing dimension can occur. Heuker et al. also reported in their study (n = 23) that patients' subjective assessment of dyspnoea correlated well with HRQoL (Heuker, Lengele et al. 2011).

Tacconi et al. noted that the main reasons for a lower HRQoL stemming from the preoperative decline in the FEV, a postoperative decline in the FVC and the extent of the chest wall resection (Tacconi, Ambrogi et al. 2012). In our study, we detected a correlation between the mean defect size and QLQ-C30, along with some limitation to breathing. In agreement with the findings from our study, Tacconi et al. observed a correlation in a decline to HRQoL measured by the SF-36 and the extent of surgical trauma (Tacconi, Ambrogi et al. 2012).

In addition, Daigeler et al. used the SF-36 instrument in their study, finding that, following chest wall reconstruction, quality of life significantly diminished compared to that amongst a general control group. Their results substantially differ from ours and also differ from those reported in other studies (Liu, Wampfler et al. 2017, Heuker, Lengele et al. 2011, Nakao, Miyata et al. 1986). Yet, Daigeler´s study amongst 36 patients did not report size of the resection, the reconstruction method or the diagnosis of patients (Daigeler, Druecke et al. 2009).

In another study amongst 68 patients, Liu et al. noted that chest wall resection with pulmonary resection did not impact HRQoL compared to pulmonary resection without chest wall resection, findings which agree with our own. However, they did not compare these results to an age- and gender-standardised general population and did not report the reconstruction method, which possibly impacted outcomes (Liu, Wampfler et al. 2017)

In spite of a high prevalence of breast cancer, a meta-analysis of chest wall–related recurrent breast cancer treatment uncovered a single study in which validated quantitative metrics were employed to analyse HRQoL (Wakeam, Acuna et al. 2017). In that study amongst a small number of patients (n = 6), the authors used the UICC performance status, finding that treatment improved HRQoL (Nakao, Miyata et al. 1986).

In the literature, no studies appeared to address HRQoL after chest wall sarcoma nor has the optimal instrument been identified for the evaluation of HRQoL following chest wall resection and reconstruction. Our study, thus, represents the first to address this important field of research with insightful and unique scientific results, which also aid in assessing the meaningfulness of surgery and patient-reported limitations in the treatment of chest wall sarcomas.

6.6 Strengths

Chest wall resection and reconstruction represents a rare and complex surgical technique. Limited knowledge exists regarding the surgical and oncological outcomes and patient HRQoL following such challenging operations. In this thesis, we analysed such outcomes in all four of our studies.

In study I, the number of patients (n = 135) is adequate, reprsenting one of the largest samples in Europe. This study included only oncological chest wall resection and reconstruction patients and, thus, the study population was more homogenous than those in other surgical series.

In studies I through IV, we classified comorbidity in patients using the CCI, allowing for a comparison of patients' prognostic comorbidities across different studies.

Furthermore, in studies I through IV, we classified surgical complications using the CD classification in order to standardise and allow for a comparison of complications.

In study I, we only excluded two patients during follow-up, with a median follow-up period reaching 49 months. The length of follow-up in studies II (39 months), III (86 months) and IV (66 months) were favourable. Given these long follow-up periods, we could calculate the 1-, 2- and 5-year overall survival of patients. Furthermore, in studies II and III, no patients were lost during follow-up.

A major strength of study IV resulted from the comparison of our results to a sample of age- and gender-standardised control population. Our sample size (n = 55) was favourable and the response rate (71%) was acceptable. Furthermore in study IV, our reporting of patient diagnoses, the extent of the surgical areas and oncological treatments extends beyond previous HRQoL studies.

6.7 Limitations

Alongside these strengths, we acknowledge several limitations to this this research. First, all four studies are retrospective and, therefore, prone to bias. The second limitation we must acknowledge involves the sample size. The sample size in study I, whilst the largest of the four studies and one of the largest in Europe, only consists of 135 patients. The number of patients in studies II and III were 21 and 49, respectively. The type of resection in study II, combining the chest, abdominal wall and diaphragm, is, however, exceptionally rare and featuring smaller numbers across all published series. In study III, the rare diagnosis of primary chest wall soft-tissue sarcoma limits the study size. This renders analysing the effects of different treatment modalities, especially various chemotherapy regimens, on outcomes extremely difficult. Overall, the lack of systematic postoperative pulmonary function tests prevented the evaluation of the impact of chest wall resection on pulmonary functioning. The number of patients, particularly in study I, could have been extended by including locally advanced lung cancers invading the chest wall. The staging, surgery and neoadjuvant and adjuvant protocols for these patients differ, however, from those included in this thesis. Therefore, we did not include this additional pool of patients. In study IV, no real impact of chest wall resection and reconstruction on HRQoL could be estimated given the lack of preoperative data collection. Finally, the heterogeneity of diagnosis or treatment and the heterogeneity in the time points of HRQoL measurement, as well as the lack of responses for various reasons could all impact the outcome of our HRQoL analysis.

6.8 Future prospects

At the beginning of the twenty-first century, computer-aided navigation as an intraoperative tool was adopted in musculoskeletal tumour surgery (Hufner, Kfuri et al. 2004). Through navigation-assisted tumour resection, encouraging results have been achieved with clear surgical margins in difficult pelvic and sacral tumour resections (Abraham, Kenneally et al. 2018). However, experiences from computer-aided navigation based on patient series and prospective randomised studies remain lacking. In future, computer-aided navigation may represent a favourable tool for oncological chest wall resections, particularly for unpalpable sternal tumours.

Different types of prostheses have been used for decades in chest wall reconstruction. For years, 3D-printing technology has been utilised in surgery, especially during surgical planning. In recent years, 3D printing has been introduced in chest wall reconstruction surgery. Experiences with 3D printing have primarily focused on either straight individually custom-made 3D-printed titanium (Vannucci, Scarnecchia et al. 2020) or polyetheretherketone (PEEK) (Wang, Huang et al. 2019) implants or a 3D-printed silicone model for an MMA prosthesis (Smelt, Pontiki et al. 2020). Results from 3D-printed implants remain preliminary and larger patient series are needed with longer follow-up times.

In addition, the histological classification of malignant tumours continues to evolve. Fortunately, knowledge and understanding of tumour behaviour are expanding rapidly. These developments may permit more personalised treatment of malignant tumours. In soft-tissue sarcoma surgery, more precise knowledge of the subtypes of sarcomas could allow for the more individualised assessment of surgical margins and adjuvant treatments.

Robot-assisted surgery (RAS) is increasingly and more widely used in urology, general surgery and gynaecological surgery. One primary benefit of RAS is the improved visualisation in a particularly confined space involving the meticulous dissection of major anatomical structures or intracorporeal dissection (Chalmers, Schlabe et al. 2018). In reconstructive plastic surgery, robotic-assisted flap harvesting has been described for latissimus dorsi (Chung, You et al. 2015) and rectus abdominis muscle flaps (Pedersen, Song et al. 2014). Thus, at present, there is a possibility that the use of RAS in flap harvesting for chest wall reconstructions. In future, however, other indications for RAS in chest wall reconstructions may be identified.

Cancer studies should include HRQoL measurements as an endpoint moving beyond the survival of patients alone. Patient-reported outcome measures, which consist of HRQoL and functional measurements, should be collected pre- and postoperatively from all surgically treated tumour patients to assess the impact of treatment on patients' lives.

In future, prospective studies are needed for the resection and reconstruction of the chest wall as well as for HRQoL amongst chest wall reconstruction patients.

7 CONCLUSIONS

Based on these clinical studies, the following conclusions can be drawn:

1. Chest wall resection and reconstruction is a safe therapeutic modality, when combined with careful patient selection, appropriate perioperative and postoperative care and an accurate surgical technique both in sarcoma and advanced breast cancer patients.

2. Our method for thoracoabdominal wall and diaphragm reconstruction proved safe without abdominal wall hernias or paradoxical chest wall movement. These combined reconstructions involved adequate stability and air-tight closure of the chest wall cavity. Diaphragm reconstruction using mesh is warranted if the diaphragm is not reattached with an acceptable tension to the chest wall.

3. This study suggests that resection with wide margins remains the primary aim for the treatment of chest wall soft-tissue sarcoma patients. If wide margins are not achieved, treatment should be combined with adjuvant radiotherapy to improve local control. Even extensive chest wall resections and reconstructions are safe therapeutic modalities. However, due to the heterogeneity of sarcomas, further research is warranted to clarify the predictive factors for subtypes of sarcoma.

4. The long-term HRQoL remains adequate and comparable to the age- and gender-standardised general population following chest wall reconstruction after oncological resection. Limitations to breathing and usual activities may occur.

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